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Proctology for the General Practitioner*

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IT is not the purpose of this presentation to offer anything new in the field of proctology, but, rather, to review certain common ano-rectal symptoms and their correlation with the evidence of examination in the establishment of correct diagnosis —a requisite for proper treatment.

The average patient is reticent to volunteer to his doctor the intimate details of his bowel habits and his ano-rectal sensations. In most instances he will limit description of his complaints to the simple statement that he has "piles." To accept this diagnosis without further interrogation and proper examination is inexcusable neglect of the responsibilities of the physician to his patient.

There is no single symptom which is pathognomonic of any specific abnormality or disease of the anal canal, rectum, or colon. Certain combinations of symptoms may be sufficiently characteristic to strongly suggest a specific disease, but diagnosis is never certain until it has been established by proper examination.

Discussion will be limited to six common symptoms: external elevations about the anus, protrusions through the anus, anal pain, anal itching, bleeding, and change in bowel habits.

ANAL ELEVATIONS

The differentiation of external elevations about the anus should be relatively simple, since they are readily accessible to direct inspection and palpation. Yet incorrect diagnosis is not uncommon, with resultant inappropriate treatment. External hemorrhoids should be readily recognized as subcutaneous varicosities which distend when the patient strains down. It is important to remember that external hemorrhoids, unless acutely thrombosed, cause no appreciable symptoms. Acute thrombosis produces a painful, tender lump which must be differentiated from a perianal abscess and a sentinel tag. These three common types of painful elevations are not infrequently confused and must be properly recognized in order to initiate appropriate treatment. Acute thrombosis of an external hemorrhoid begins with sudden pain and simultaneous development of a tender lump at the anus. The patient can tell, usually, not only the day but the hour when this occurred. Symptoms reach a maximum intensity quickly, and begin to regress within a few days. In the case of a perianal abscess, pain precedes any evidence of external swelling by hours or days. Symptoms are progressive unless spontaneous rupture of the abscess occurs. A sentinel tag, often incorrectly called a "sentinel pile," is an acute inflammatory elevation of skin distal to a fissure-in-ano. Pain with bowel movements has usually been present for days or weeks before the development of a tender elevation at the anus.

Differentiation between these three conditions should never be difficult on physical examination. Acute thrombosis of an external hemorrhoid produces a sharply localized, firm, rounded elevation, usually with a bluish discoloration, although at times this discoloration may be hidden by edema between the thrombosis and the overlying skin. The usual sites for occurrence of thrombosis are in the two posterior and the right anterior quadrants. The elevation of a perianal abscess is less sharply demarcated, and palpable induration has a less distinct edge. Fluctuation may be present, but is not usually evident until the abscess has reached maturity and is about to rupture through the skin. The overlying skin may or may not show an inflammatory red-

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ness, with none of the bluish discoloration of a thrombosis. Abscesses may occur in any quadrant, within or without the anal verge. A sentinel tag usually occurs in the posterior or anterior midline, most commonly posteriorly. It is a firm, cone-shaped tag of indurated skin, usually with a perpendicular wall on the side of the cone toward the anal canal. Proximal to the tag there will be found an anal fissure.

Treatment of a thrombosed external hemorrhoid may be palliative or surgical. It will always subside, with any form of treatment or with no treatment at all. Surgical excision, not incision, is indicated when this will effect a definite shortening of the period of suffering and disability of the patient. Conservative treatment consists of frequent sitz baths to relieve sphincter spasm and to hasten absorption, and mechanical lubrication to diminish the irritation of friction. For this there is nothing better than plain vaseline.

Treatment of a perianal abscess should be immediate incision and drainage. Delay until fluctuation is present allows further destruction of tissue and increases the probability of subsequent fistula formation. The direction of the incision should be tangential or circumferential rather than radial.

Recognition of a sentinel tag directs treatment to the fissure-in-ano, since the tag is secondary to the fissure.

Other types of external elevations which deserve consideration, but which can only be mentioned in this general discussion, include epithelioma, condyloma acuminata, tuberculosis, chancre, chancroid, furuncle, infected sebaceous gland, and the external opening of a fistula-in-ano.

ANAL PROTRUSIONS

Protrusions through the anal canal from within should be immediately differentiable from external elevations by the fact that these are covered with mucus membrane rather than skin, with one exception. This exception is an hypertrophied anal papilla which has become so large that it everts through the anal canal to the outside. Such an hypertrophied papilla is usually firm and rounded at the tip. It is the result of a low-grade inflammatory process secondary to a chronic anal cryptitis. It is not a precancerous lesion, but can be a source of considerable annoyance to the patient.

Treatment consists of simple amputation, in some instances with simultaneous excision of an associated deep infected anal crypt.

The commonest type of anal protrusion is that of internal hemorrhoids. These are usually seen as quadrant protrusions, containing obvious varicosities, with the covering mucosa almost always showing evidence of ulceration.

Rectal prolapse may be incomplete or complete. Incomplete prolapse consists of protrusion through the anal canal of the mucous membrane of the rectum, while complete prolapse consists of protrusion of all layers of the rectal wall. Differentiation of the two types is readily made by inspection. In simple mucosal prolapse, longitudinal folds radiate outward from the center of the spherical-shaped protrusion. In complete prolapse, the protrusion tends to be oval in shape, with the mucous membrane thrown into circular folds.

A simple and satisfactory treatment for incomplete prolapse is submucosal injection of 5 per cent quinine and urea hydrochloride, or 5 per cent phenol in vegetable oil. Correction of complete prolapse is much more difficult. It is apparent from the great number of surgical procedures advocated that there is no entirely satisfactory method of surgical repair. Many cases of complete prolapse can be adequately corrected by an injection technic in which from 100 to 400 cc. of 1:3000 hydrochloric acid solution is injected into the pelvi-rectal spaces. This produces a fibrous tissue reaction which aids in supporting the rectal wall. At the same time multiple submucosal injections of 5 per cent phenol in oil should be done, with subsequent repetition of the latter procedure whenever there is any evidence of prolapse.

Adenomatous polyp of the rectum and even of the sigmoid may protrude through the anal canal. It is particularly important in the patient who gives a history of anal protrusion but who cannot demonstrate the protrusion at the time of examination, that adequate inspection of the rectum and lower sigmoid be made by proctoscopic examination to rule out this possibility. Such a polyp is a definite pre-cancerous lesion, which should be recognized and removed.

A polypoid carcinoma of the rectum may protrude through the anal canal by direct extension of growth, or by actual prolapse. The importance of recognition in such a case is obvious.

ANAL PAIN

Pain in the region of the anal canal may be due to a variety of conditions which can be differentiated only by suitable examination. The presence of hemorrhoids is not the cause of pain unless acute thrombosis is present. The commonest causes of pain are due to infection originating in the anal crypts of Morgagni. Localized inflammation in these crypts may cause a variable degree of anal discomfort and sphincter spasm. Diagnosis is dependent upon visualization of the muco-cutaneous line by means of an anoscope. Extension of infection from an anal crypt may produce a chronic fissure-in-ano, a perianal abscess, and a fistula-in-ano.

The pain of a fissure-in-ano is brought on by bowel movement and may persist for a few minutes, for several hours, or even until the next bowel movement. Diagnosis is frequently possible by external inspection, particularly when a sentinel tag is evident. Recognition of a fissure in the upper end of the anal canal may be possible only by anoscopic examination.

The pain of a perianal abscess is constant, and unaffected by bowel movement. In the early stage of development an abscess sometimes is not evident upon external inspection or external palpation. An important diagnostic procedure is bi-digital palpation of the perianal tissues, with the index finger

inserted into the rectum and flexed to oppose the thumb outside the canal. Palpation of a deep area of tender induration by this means is indication for prompt incision and drainage.

Pain related to a fistula-in-ano is evidence of inadequate drainage of an area of acute infection somewhere in the course of the fistulous tract. The establishment of adequate drainage is of importance in order to prevent further extension of infection and development of a more complicated fistula. Fistulectomy is necessary for permanent cure.

Less common causes of anal pain include epithelioma, gonorrheal cryptitis, chancre, chancroid, condylomata acuminata, tuberculosis, and sacrococcygeal spasm.

PRURITUS ANI

Itching about the anus is a common symptom, at times of such intensity that it seriously interferes with normal activity and sleep. There are many diverse theories of etiology and methods of treatment. Pruritus ani is frequently discussed as a syndrome, rather than as a symptom. Anal itching is subliminal pain, due to mild stimulation of local sensory nerves. The objective of treatment is to identify the cause of this local sensory stimulation and to remedy it. The cause may be a fungus infection of the perianal skin, or a phytid reaction to some distal focus of fungus infection. Anal cryptitis, a hypertrophied anal papilla, a fissure, or a fistula may be responsible. The presence of hemorrhoids may be a factor, particularly if the protrusion of an internal hemorrhoid into the anal canal results in excessive moisture with resultant maceration and irritation of the skin. Scratching often becomes a significant factor in the persistence or aggravation of a perianal dermatitis.

In our experience, anal cryptitis and perianal dermatitis, the latter quite commonly of fungus origin, are the two commonest causes of pruritus ani. In many hundreds of cases, we have never seen a patient with pruritus ani who failed to show some local abnormality on examination. We have not cured every patient with anal itching. But in every patient in whom it has been possible to eradicate the local cause of abnormal sensory stimulation, itching has been relieved.

BLEEDING

The significance of the passage of blood through the anus cannot be known until the source of such bleeding has been accurately determined. The cause may be transient and trivial, or it may be a threat to life itself. The source may be located in the anal canal or at any level in the gastro-intestinal tract.

Certain features in the characteristics of bleeding are of aid in determining the site of the responsible lesion. The dripping of blood after bowel movement, or unexpected external soiling by blood is usually due to a lesion which is located below the grasp of the sphincter muscle. Associated anal discomfort suggests a lesion distal to the mucocutaneous line, since this line represents the upper limit of sensory innervation. Blood immediately following bowel movement and on the toilet paper suggests a lesion of the anal canal or rectal ampulla. Streaks of blood on the surface of a formed stool suggests a localized ulcerative lesion in the sigmoid or rectum. Mixed blood in an unformed stool may be from any level of the rectum or colon, or from even higher in the intestinal tract.

In general, the passage of bright red blood suggests a lesion distal to the sigmoid, while dark blood suggests a lesion proximal to the rectosigmoid. However, exceptions to this generalization are not infrequent. Profuse hemorrhage from a lesion as far back as the duodenum, with very rapid progress of the blood through the intestinal tract, may result in the passage of blood which is still fresh in appearance. And old dark blood may come from internal hemorrhoids, accumulating in the rectal ampulla after one bowel movement, to be passed with the next movement.

In every patient with bleeding investigation should include a digital, anoscopic, and proctoscopic examination. The mere presence of hemorrhoids should not be accepted as the cause of bleeding without proctoscopic examination to rule out the possibility of ulcerative disease of the rectal mucosa, and particularly to rule out the presence of a polyp or carcinoma. The innumerable instances in which treatment of hemorrhoids has been undertaken in complete ignorance of the presence of a cancer only a few inches away comprise one of the most tragic phases of the war against cancer. It should never be forgotten that cancer is more common in the colon and rectum than in any other organ of the body common to both sexes, except the skin. Fifty per cent of the cancers of the colon and rectum are within reach of the examining finger, and 70 per cent are within reach of a proctoscope.

Benign adenomatous polyps are a frequent cause of bleeding. Such polyps are pre-cancerous lesions. Their discovery before malignant degeneration takes place permits local removal of the lesion, and prevents the development of a cancer.

When anoscopic and proctoscopic examination fails to demonstrate the source of bleeding, or whenever the character of the bleeding is such that a higher lesion is suspected, barium enema examination is indicated. The technic of this examination should be such that it will demonstrate not only the presence of a carcinoma, but of a benign adenomatous polyp. The use of air contrast examination is essential in the demonstration of the majority of polyps of the colon. Even with the best technic, x-ray examination has a diagnostic accuracy of only about 90 per cent. A second and even a third examination is indicated when the clinical evidence points toward a diagnosis of polyp or carcinoma.

Demonstration of lesions proximal to the colon requires x-ray examination by barium meal.

CHANGE IN BOWEL HABITS

A change in bowel habits in any adult should be considered presumptive evidence of malignancy of

the colon until other diagnosis has been established and carcinoma has been ruled out by adequate examination. A diagnosis of "intestinal flu" frequently delays recognition of the presence of a carcinoma for weeks and months. A diagnosis of ulcerative colitis cannot be established without proctoscopic or x-ray examination. The demonstration of diverticulosis by x-ray examination is acceptable as the explanation of disturbance of bowel habits only when the roentgenologist has ruled out the possible presence of a co-existing carcinoma. When change in bowel habits is accompanied by blood in the stool, particular care must be taken to rule out the possible presence of a polyp or of a carcinoma before accepting diverticulitis as the cause of symptoms. Barium enema examination should be repeated if bleeding persists.

CONCLUSION

With any symptom referable to the colon or rectum, the establishment of correct diagnosis by adequate examination is a requisite to proper treatment. Bleeding and change in bowel habits are the two cardinal symptoms of malignancy. Any other diagnosis should be made, in every instance, only after the exclusion of malignancy as the cause of these symptoms by adequate examination.

Blood Protein Depletion in Infantile Eczema*

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IN a study of infantile eczema conducted at the Los Angeles County General Hospital since January, 1941, nutritional crises [27] were observed in infants suffering from severe generalized eczematous involvement. These crises were introduced by a sudden gain in weight (occult or manifest edema), sudden loss in weight (dehydration), apathy and listlessness, anorexia, profuse diarrhea, or actual prostration.

To evaluate this syndrome more completely, routine hemoglobin and albumin-globulin determinations were made upon admission of every infant to the eczema service. These determinations were repeated at weekly intervals until discharge from the hospital.

The incidence of hypoproteinemia was at first startling, then recognized as a frequent complication in a metabolic derangement which regularly included deficient food intake (elimination diets and, or failure of complete absorption) and excessive food loss (allergic diarrhea). The comparative infrequency with which this picture is mentioned throughout the literature and the frequency with which it is encountered with routine determinations furnished the basis for this study.

A brief summation of a few facts concerning protein metabolism aids considerably in a more complete appreciation of the entire picture.

The average blood levels for infants up to three months of age is 5.5 gm. per cent for total proteins, 3.6 gm. per cent for albumin and 1.8 gm. per cent for globulin.[6]

In those from three months to two years of age, average reported levels are 6.2 gm. per cent for total proteins, 4.3 gm. per cent for albumin and 1.9 gm. per cent globulin.

In the premature,[3] blood protein values are even lower. Such apparent globulin deficiency may be hypothecated on a lack of immunologic stimuli and consequently diminished globulin production. This is somewhat substantiated by the increase of globulin values in septic states.

Chronic hypoproteinemia in a group of children without apparent illness was found in Tennessee.[6,17]

Younger children because of their low blood protein levels are reported to show increased susceptibility to illness and to nutritional edema.

Hypoproteinemia may be divided into prehepatic, hepatic and posthepatic varieties. In the prehepatic type there is interference with intake, digestion or absorption of food.

In the hepatic variety there is actual inability of the liver to synthesize protein despite an adequate supply of protein building material. In the posthepatic type there is abnormal loss despite adequate supply and synthesis.

It is generally agreed that the liver [4,9,11,17] is the major source of plasma protein production. Fibrinogen is completely formed in this organ. The reticuloendothelial cell system provides the source of most of the globulin which actually comprises a number of separate fractions.[22] The chief depots of the reticuloendothelial cell system are found in the liver, bone-marrow and skin.

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Protein levels are described as fluid, maintaining a constant balance among (a) liver, (b) blood, (c) tissue cells.[13] Decreased plasma protein is accompanied by tissue protein depletion. During deficiency states approximately 30 times as much nitrogen is lost from tissue protein as from serum protein.

The forces which tend to retain protein in circulation or cause its return to the circulation are (1) osmotic pressure (determined by albumin, globulin and crystalloid blood content)[1,8,11] and (2) capillary hydrostatic pressure (falls as it proceeds through capillaries, thus provided a differential fluctuating value which in turn produces a state of ebb and flow).

Plasma albumin possesses a relatively small molecule. It contributes most in maintaining osmotic pressure. One gram of albumin will attract 15 cc. water from tissue exerting 5.5 mm. pressue of mercury. One gram of globulin exerts a pressure of 1.4 mm. mercury. Twenty-five grams of albumin is equivalent in osmotic pressure to 420 cc. normal plasma. The total plasma proteins exert an osmotic pressure of 21-29 mm. mercury.[19] The critical edema level has been estimated at:[18,26]

5.5 ± 0.3 gm. serum protein
2.5 ± 0.2 gm. albumin

At this level the capillary hydrostatic pressure exceeds the vascular osmotic pressure with the escape of fluid from the vascular bed causing edema.

For the restoration of plasma protein values, plasma, blood and amino-acids both orally and parenterally and parental liver extracts were employed. Approximately one thousand cubic centimeters of plasma is needed to raise the blood protein one gram per one hundred cubic centimeters. Thus maintaining plasma protein levels solely with plasma would be obviously impractical.[7]

Two commercially obtainable amino-acid mixtures were used. One is stated to be an "enzymic digest of casein and pancreas containing amino acids and polypeptides, with all of the essential amino acids."* This product was used subcutaneously and intravenously. The second which proved more palatable is stated to be a protein hydrolysate "of beef, wheat and milk"† (enzymatic).

Approximately 30 grams of amino acids daily is recommended for children in the intravenous treatment of protein deficiency.[6]

Amino acids deemed necessary to build plasma protein are:[21]

valine	methionine
leucine	tryptophane
isoleucine	histidine
phenylalanine	lycine
arginine	threonine

Although sensitivity is regarded as absent to protein breakdown products below the proteose stage,[2] definite sensitivity was seen in several infants given these preparations by either route.

Growth stimulus or "growth factor" is recognized more easily in proteins which simulate body proteins. Lactalbumin which comprises 60 per cent of human milk resembles body protein closely.[23,24] Vegetable protein has proved half as valuable as animal protein, restoring plasma protein and reducing edema.[12] Gelatin furnishes protein which is deficient in tryptophane[25] and sulfur-containing amino acids but with other incomplete proteins is valuable because of reciprocal supplementation,[16] one supplying what another may lack.

Protein need in the infant is proportionately greater than in the adult because of the increased rate of growth.[6] The amount of protein required depends on its digestibility, availability of amino acids, and its quality (biologic value or the percentage of absorbed nitrogen). Varying digestibility indices have been offered with the following in a descending scale of values: Milk, 98 per cent; meat, 97 per cent; cereal, 85 per cent; legumes, 78 per cent; fruits, 85 per cent; vegetables, 83 per cent.

Human milk contains less protein than cow milk but because of a high lactalbumin content less is needed for growth. Two to two and one-half grams of human milk protein per kilogram of body weight, as compared with two and a half to three and a half grams of cow milk protein per kilogram, are required for optimum nutrition. Actually the amount of cow milk usually used in routine formulas ranged between three and a half to four and a half grams of protein per kilogram per day (one and a half to two ounces of milk per pound of body weight per day).[14]

The protein of human milk supplies about nine per cent of the daily caloric intake. The protein of cow milk, because of its lactalbumin deficiency, must be fed in larger quantities and should supply about 16 per cent of the caloric intake when fed in optimum amounts.

It has been suggested that liver extract and vitamin B parenterally will raise the vitamin A absorption level in the blood.[15]

Because of the low vitamin A absorption in infantile eczema[5] which partially accounts for the increased susceptibility of these infants to upper respiratory infections, such therapy was initially offered to a few of the infants studied. Increased growth increment, longer intervals of freedom from infection and more easily maintained protein balance occurred so regularly that in the protein deficient group where nutrition was at its poorest this therapy was made routine from the time of admission to discharge. Whether there was an original liver dysfunction which aided in the production of a secondary hypoproteinemia or whether the hypoproteinemia produced liver dysfunction—parenteral liver therapy seemed indicated.

Hemoglobin values were originally requested with each plasma protein determination to assess hemoconcentration and to ascertain whether blood or plasma was to be used in therapy. Hematocrit values have since been added to the routine procedure as a more accurate index of hemoconcentration. Even with such determinations, it is conceivable that in an anemic hypoproteinemic infant who is considerably dehydrated, hypoproteinemia might be completely

*Amigen—Mead-Johnson & Co.
†Aminoids—Arlington Co.

masked by an elevated hematocrit and a normal protein reading.

The body favors hemoglobin formation over plasma protein restoration,[20] possibly because of the normally higher percentage of hemoglobin as compared with plasma protein and because plasma proteins furnish a portion of the precursor substances for the production of hemoglobin. Throughout the series of infants observed, protein fortification was pursued until both hemoglobin and plasma protein values returned to fair levels and the infant "appeared well."

The use of milk substitutes was discovered whenever protein deficiency was present, because of the increased incidence of nutritional crises which tended to occur when milk was removed from the dietary. The increased incidence of crises on milk-free regimes is partially explained by the fact that cystine is relatively high in lactalbumin and is also a key amino acid in plasma protein production. When it was absolutely necessary for such withdrawal, more frequent parenteral liver extract appeared to aid in maintaining a progressive weight gain.

Edema is a secondary manifestation of hypoproteinemia and was observed in our series both as occult (sudden increase in body weight) and manifest (obvious swelling of portions of the body).

Infections with suppuration cause a post-hepatic hypoproteinemia. The estimated range of loss has been stated as:

8.1—21.00 grams per hundred cubic centimeters total protein.
4.6—11.5 grams per hundred cubic centimeters of total albumin.

Infection also reduces the protein regenerating ability of the liver and may even alter the permeability of the capillaries, thus enhancing the possibility of edema. Whole blood is better than plasma when infection is present because it also aids in combating the disease process.[22]

Vitamin therapy is of importance in protein metabolism. Vitamins B-1 and C deficiencies may complicate hypoproteinemia. Vitamins A and B deficiencies have been reported as productive of an eczematoid dermatitis.

The picture of protein deficiency in the infant typically includes:

1. Anemia
2. Failure to gain
3. Lowered resistance to infection
4. Flabby musculature
5. Deficiency of plasma proteins possibly productive of edema.

THERAPY

Liver extract 0.5 cc. (7.5 units) to six months and 1 cc. every six months of age intramuscularly twice weekly.

Vitamin B complex 1 cc. intramuscularly twice weekly.

Intravenous plasma once weekly when total blood protein values fell into range 5.5 - 6.0 gm.: twice weekly when values were below 5.5 gm.

Intravenous blood was alternated with plasma when hemoglobin values were low.

One tablespoon twice daily of hydrolyzed amino-acid mixtures were included in daily dietary.

Diet eliminations were followed as summarized in another paper.[27]

PROCEDURE OF EXPERIMENT

A random sample of 54 cases of infantile eczema (38 boys and 16 girls, all 91 days of age or over at time of admission) was studied to determine the percentages of deficiency. The following percentages were found:

Albumin	.25 ± .058
Globulin	.37 ± .066
Total Protein	.26 ± .060

STATISTICAL INTERPRETATION

The cases showing protein deficiency were examined to find (1) whether albumin or globulin showed a greater per cent of deficiency, (2) which of the two proteins was restored first and by how much. The results are shown in Table 1.

TABLE 1—*Comparison between albumin and globulin deficiency on basis of percentage of deficiency and number of days from time deficiency was noted until recovery.*

PERCENTAGE OF DEFICIENCY FROM NORMAL*

	Albumin	Globulin	Total Protein
Number of cases	13	20	14
Median	0.12	0.21	0.11
First quartile	0.05	0.11	0.05
Third quartile	0.22	0.25	0.20
Quartile range	0.17	0.14	0.15
Mean	0.16±.04	0.21±.02	0.15±.03
Standard deviation	0.15	0.10	0.13
Difference between means	0.05		
Standard error of the difference of two means	0.047		
Level of significance	0.310		

NUMBER OF DAYS TO RECOVERY

	Albumin	Globulin	Total Protein
Number of cases	11	20	14
Median	36.0	13.5	24.0
First quartile	21.0	8.0	8.8
Third quartile	69.0	38.3	54.5
Quartile range	48.0	30.3	55.7
Mean	45.7±9.2	24.3±5.2	36.6±8.4
Standard deviation	30.4	23.2	31.4
Difference between means	21.4		
Standard error of the difference of two means	10.53		
Level of significance	0.074		

* Normal grams per 100 cc. of blood; albumin 2.3, globulin 1.9, total protein 6.2.

(1) These results indicate that there is a tendency for the globulin fraction to show a greater percentage of deficiency from normal than the albumin. Both the median and the mean for globulin deficiency as a percentage of normal are higher than for albumin. On the other hand, both the quartile range and stand-

ard deviation indicate that the data is extremely variable. This high degree of variability in each of the small samples is reflected in the standard error of the difference between the two means of .047. This is about as large as the difference between the two means of .05. The high degree of variability produced a level of significance of .31. In short, 31 samples out of 100 picked at random from the same universe would show a difference as great as or greater than that shown between the per cent of albumin and globulin deficiency. The difference between albumin and globulin deficiency is not significant. A larger sample is necessary to draw reliable conclusions concerning this aspect of protein deficiency.

(2) Findings indicate quite conclusively that globulin deficiency is dissipated faster than albumin deficiency. The standard deviation is .67 of the mean for albumin and .95 for globulin. The difference between the means is significant as indicated by a level of significance of .074. This indicates that in only 7.4 pairs of samples out of a hundred taken from the same universe would differences as great as that shown appear.

DISCUSSION

The incidence of protein deficiency in a random sample of infantile eczema cases averages 26 per cent. The comparatively greater depression of globulin values is interesting in the designation of body tissues most affected, viz., the reticulo-endothelial cells with large depots in the skin and liver. This in turn points out a therapeutic approach in at least correcting the deficiency state.

The high incidence of protein deficiency makes it imperative that blood protein values be routinely investigated in the study and therapy of infantile eczema whether such work is conducted in the office or in the hospital.

The age range of the infants studied was not selected but represented the group when first admitted to the Los Angeles County Hospital eczema ward. With the exception of three other protein deficiencies, all infants studied fell into this range. A similar group of private cases almost wholly fell into the age range of under 90 days. This group will be reported in another paper. Findings, however, apparently do not materially differ from those here presented.

Knowledge of such striking protein deficits has aided and will aid in eliminating deaths occurring in previously described nutritional crises.

Work done to the present time merely emphasizes the need for more intensive and complete investigation.

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REFERENCES

1. Cohn, E. J.: The plasma protein: Their properties and function, trans. and studies, Coll. of Physician, 10:149—1942.

2. Cooke, R. A.: Protein derivatives as factors in allergy, Annals of Internal Medicine, 71-80, Vol. 16 (No. 5, Vol. XXI) (June), 1942.

3. Darrow, D. C., and Cary, M. K.: Serum albumin and globulin of newborn, premature and normal infants, J. Pediat., 3:573-579 (Oct.), 1933.

4. Davis, H. A., and Getzoff, P. L.: Hypoproteinemia in surgical diseases, Archives of Surgery, Vol. 44, No. 6 (June), 1942.

5. diSont 'Agnee, P. A., and Larkin, D. F.: Vitamin A absorption in infantile eczema, Proc. Soc. Exptl. Biol. & Med., 52:343-344 (April), 1943.

6. Dodd, K., and Minot, A. S.: The occurrence of moderately reduced serum albumin in five hundred children in a southern clinic, J. Pediat., 8:452-438 (April), 1936.

7. Gardner, Jr., C. E., and Trent, J. O.: Intravenous amino acid administration in surgical patients using an enzymatic casein digest, Surg. Gynec. & Obst., 75:657-660 (Nov.), 1942.

8. Govaerts, M. D.: Influence de la Teneur du serum en albiemimes et en globulines sur la pressim osmotique des proteins et sur la formation des oedemes; Bull. Acad. Roy. Med., Belg., 13:356, 1927.

9. Jones, T. B., and Smith, H. P.: The blood fibrinogen level in hepatectomized dogs and an outline of a method for the quantitative determination of fibrinogen, Am. J. Physiol., 94:144-161 (July), 1930.

10. Keys, A: Colloidal dimensions, thermodznamec activity and the mean molecular weight of the mixed proteins in blood serum, J. Physical Chem., 42:11-20, 1938.

11. Knutti, R. E., Erickson, C. C., Madden, S. C., Rekers, P. E., and Whipple, G. H.: Liver function and blood plasma protein formation, J. Exptl. Med., 65:455, 1937.

12. Lui, S. H., Chu, H. I., Wang, B. H., and Chung, H. L.: Nutritional edema, effect of level and quality of protein intake on nitrogen balance, plasma proteins and edema, Proc. Soc. Exptl. Biol. and Med., 29:250-252, 1931.

13. Madden, S. C., and Whippel, G. H.: Plasma proteins: Their source, production and utilization, Physiol. Rev. 20:194-215 (April), 1940.

14. Marriott, W. M., Jeans, P. C.: Protein metabolism, infant nutrition, C. V. Mosby Co., 48-53, 1941.

15. May, C. D., McCreary, J. F., Blackfan, K. D.: Notes concerning the cause and treatment of celiac disease, J. Pediat., 21:289-305 (Sept.), 1942.

16. McCollum, E. V., Orent-Keiles, E., and Day, H. G.: Ch. 6, nutritional value of proteins and the effects of variations in the level of dietary proteins, The Newer Knowledge of Nutrition, 5th Ed., MacMillan Co., 120-154, 1939.

17. McMaster, P. D., and Drury, D. R.: The source of fibrinogen, Proc. Soc. Exptl. Biol. Med., 26:490, 1928-1929.

18. Moore, N. S., and Van Slyke, D. D.: The relationships between plasma, specific gravity, plasma protein content and edema in nephritis, J. Clin. Investigation, 8:337-355, 1930.

19. Newhouser, L. R., and Losner, El.: Use of human albumin in military medicine, U. S. Nav. Med. Bull., 40:796-799 (Oct.), 1942.

20. Robscheit, F. S., Robbins, Miller, L. L., Whipple, G. H.: Hemoglobin and plasma protein, J. Exptl. Med., 77:375-396 (Apr.), 1943.

21. Rose, W. C.: The nutrative significance of the amino acids, Physiol. Rev., 18:109-136 (Jan.), 1938.

22. Savin, F. R.: Cellular reactions, to a dye protein, with a concept of the mechanism of antibody formation, J. Exptl. Med., 70:67-81, 1939.

23. Sherman, H. C.: Amino acids in protein molecule, Chemistry of Food and Nutrition, Ch. IV, 56-70, McMillan Co., 1937.

24. Schmidt, C. L. A.: The relation of the amino acids to products of biochemical importance, the chemistry of the amino acids and proteins, Ch. V. P. 221, Charles C. Thomas, 2nd Ed., 1944.

25. Schoenheimer, Ratner: Metabolism of proteins and amino acids.

26. Weech, A. A., and Ling, S. N.: Nutritional edema. Observations on the relation of the serum proteins of the occurrence of edema and to the effect of certain inorganic salts, J. Clin. Investigation, 10:869-888 (Oct.), 1931.

27. Wolpe, L. Z: Three year review of infantile eczema at the Los Angeles County Hospital (unpublished data).

The Blalock Operation for Congenital Pulmonary Stenosis*

H. Brodie Stephens,† M.D., *San Francisco*

Blalock and Taussig in May, 1945, introduced a shunt, or by-pass operation for the treatment of the most frequently encountered type of congenital cardiovascular defect accompanied by cyanosis. This defect goes under the term "Tetralogy of Fallot" and is characterized by pulmonic stenosis or atresia, interventricular septal defect, dextroposition or overriding of the aorta, and right ventricular hypertrophy.

Subsequent communications by Blalock [2,3,4] have demonstrated the extreme value of the shunt operation in the management of those congenital cardiovascular defects where there is an inadequate flow of blood to the lungs. In addition, Blalock has demonstrated that one of the branches of the aortic arch can usually be connected to a pulmonary artery without encountering insuperable difficulty; that cyanotic children withstand anesthetization and temporary occlusion of one pulmonary artery; and finally, that the subclavian artery can be divided within the thorax and the collateral circulation to the arm remains adequate.

Taussig and Blalock emphasize two important diagnostic criteria in establishing the diagnosis of insufficient pulmonary blood flow. These are (1) roentgenographic evidence that the pulmonary artery is diminutive in size and (2) clinical and roentgenographic evidence of absence of congestion in the lung fields. Another clinical point worthy of note is that the heart is either normal in size or relatively small in cases of the tetralogy of Fallot.

Dr. Blalock mentions methods developed by Dr. Richard Bing by which blood flow through the pulmonary arteries, and systemic blood flow, can be determined with a fair degree of accuracy. These methods have been of diagnostic value in the doubtful cases. We have not had the opportunity to do any blood gas analyses at the University of California Hospital but have relied heavily upon Dr. Earl Miller of the Radiology Department. Dr. Miller has perfected the technic of angiocardiography to a high degree of accuracy and we consider diodrast cardiograms an essential part of the work-up of each patient that is a possible candidate for the Blalock operation.

Blalock states that the preferable age for his shunt operation is from three to ten years. He prefers an end to side union of the subclavian artery to one of the pulmonary arteries. The subclavian branch of the innominate artery is the vessel of choice since this vessel makes a less acute angle with its parent artery after the anastomosis is performed. The thoracic incision is made on the side opposite to that on which the aorta descends. The aorta descends on the right rather than the left in approximately one patient in five. The innominate artery arises on the side opposite to that on which the aorta descends.

Recently Potts [5] and his group have advocated anastomosing the aorta to the left pulmonary artery employing an ingenious clamp that occludes only a portion of the aortic lumen. The chief advantages of Potts' operation are that the size of the shunt can be accurately determined and, in addition, a union between the aorta and the pulmonary artery would in all likelihood be technically simpler and more likely to function in patients past 20 years of age than the one in which the subclavian artery is used. When a patient has attained most of his growth the gap to be bridged is greater in proportion to the length of the artery.

We have adopted the use of the water manometer to measure the pulmonary artery pressure as advocated by Dr. Blalock. The pulmonary artery pressure is always measured at the operating table if the artery appears abnormally large or is pulsating. Blalock states the pulmonary artery pressure is below 240 mm. of water in the great majority of his cases. In addition, Blalock believes an anastomosis is probably inadvisable if the pulmonary artery pressure is greater than 300 mm. of water.

Twenty-eight cases are being reviewed in this communication. All the patients were operated upon at the University of California Hospital and it was our opinion they had a reasonable chance of being benefited by the Blalock operation. The length of time of observation since operation extends from 14 months to one month; the last operation in this group was performed on the 28th of March, 1947.

Table I shows the sex and age of the patients at the time of operation. More recently the Blalock procedure was performed on a patient (male) of 35 years of age and early observation indicates that this patient will receive considerable benefit from the operation.

Table I.—*Blalock Procedures*

Number of cases:		
Females	12	
Males	16	
Total Cases		28
* * *		
Patients observed from 14 months to 1 month postoperative:		
Oldest in group	30 yrs.	
Youngest in group	5½ mo.	
Age of patients at time of surgery:		
0– 3 yrs.	11	
3–10 yrs.	11	
10–20 yrs.	5	
30 yrs.	1	

* Read before the Section on General Surgery at the 76th Annual Session of the California Medical Association, Los Angeles, April 30-May 3, 1947.

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Table II designates the appearance time of cyanosis. It will be noted that in seven of the patients cyanosis appeared first in from a few days to four months after birth. It is possible the cyanosis that appeared in this particular time period may have followed the spontaneous closure of the ductus. The late appearance of cyanosis in the two older patients is rather to be expected since individuals living to this age must, of necessity, have less pulmonary stenosis than the younger individuals that require hospitalization in the early years of life.

Table III outlines the reasons for not doing the shunt operation in six cases. Figure 1 is the artist's drawing of the anomalous vessel found in Case 1 of this group. This vessel arose from the aorta and functioned as a patent ductus. There was no pulmonary artery take-off from the right ventricle. The anomalous vessel functioning as a patent ductus was temporarily occluded on the operating table but the heart would fail in a matter of 15-20 seconds and accordingly the operation was terminated without any attempt to add more blood to the pulmonary arteries as there was sufficient blood going to the lungs through this anomalous vessel.

TABLE II

Cyanosis First Noted:	
At birth	12
From birth—4 mos.	7
4 mos.-5 yrs.	9*

* Cyanosis appeared in the patients aged 20 and 30 years at 5 years and 2 years, respectively.

TABLE III

Total cases explored	28
Total cases receiving shunt	22

Reason for no shunt in 6 cases:

1. 7½-year-old male—anomalous vessel from aorta recognized at surgery. (Expired 6 hours P.O.)
2. 4¾-year-old female—anastomosis could not be done—heart stopped each time right pulmonary artery was occluded. (Expired 5 hours P.O.)
3. 7-year-old male—early case, pulmonary artery appeared normal size—did not measure pressure or size of vessel. This patient, perhaps needed operation.

	Pulmonary artery pressure	Size†	Sex	Age
4.	760 mm. saline	19 mm.	M	4½ yrs.
5.	370 mm. saline	25 mm.	M	2½ yrs.
6.	500 mm. saline	15 mm.	F	5½ mo.*

* This patient died a few hours P.O. Heart would fail each time right pulmonary artery was occluded. Postmortem revealed transposition of great vessels, two intraventricular defects; small patent ductus.

† Diameter of pulmonary artery as measured by calipers at operating table.

The case of patient 2, Table III, represented a complete atresia of the pulmonary artery take-off; a small patent ductus was the only conduit by which blood could reach the lungs for aeration. There was an ante mortem thrombus in the left pulmonary artery hence each time the right pulmonary was temporarily occluded, the heart would begin to fail.

Cases 4, 5, and 6, Table III, all represent abnormally high pressures in the pulmonary system and probably would have received no improvement from the Blalock operation. It is quite possible in case 6 (Figure 2), that there was a reversal of flow through the patent ductus as this shunt, plus the interventricular septal defects, were the only connections between the greater and lesser circulatory systems.

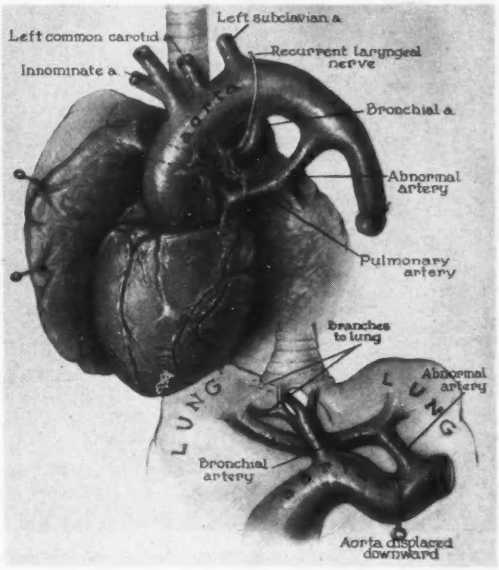

Figure 1.—Additional description of this case is in the text (Case 1, Table III). This anomaly could probably be classified as a truncus arteriosus with enlarged bronchial arteries.

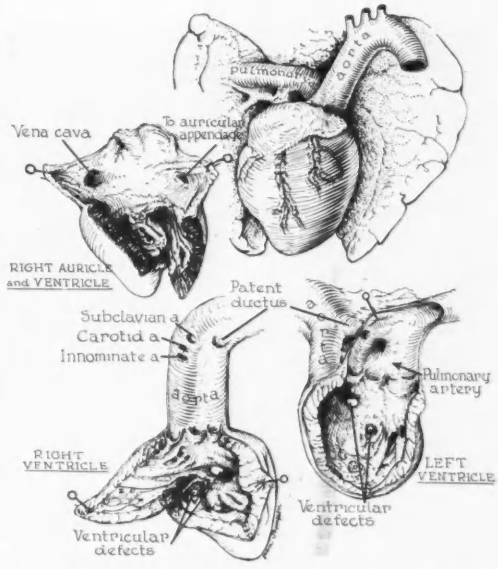

Figure 2.—Case 6, Table III. Complete transposition of the great vessels with a patent ductus arteriosus.

All the patients in the group have had preoperative diodrast cardiograms (Figures 3 to 7) studies and electrocardiographic tracings. The diodrast cardiograms are not unequivocal but they give valuable information particularly as concerns the degree of cross chamber mixing and overriding of the aorta. The electrocardiograms characteristically shows right ventricular hypertrophy in a very high percentage of the cases with pulmonic stenosis.

Table IV, shows the number of times the different

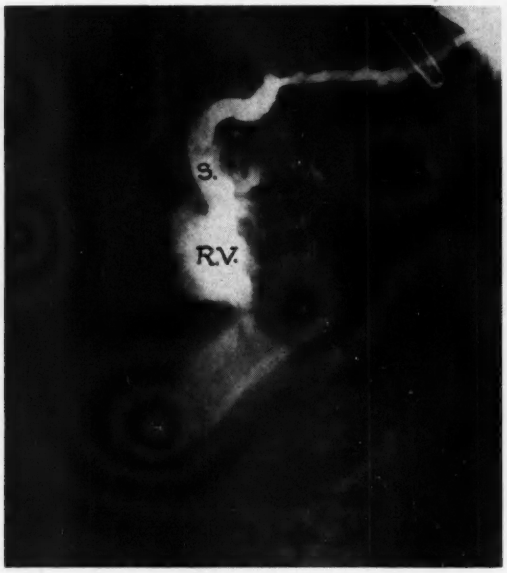

Figure 3.—(a) Left lateral oblique diodrast cardiogram. S—Superior vena cava, A—Aorta, P.A.—Pulmonary Artery, R.V.—Right Ventricle, L.V.—Left Ventricle (these abbreviations will be used throughout cardiograms.) The overriding is poorly shown in oblique film, much better demonstrated in Figure 3(b). Note the absence of cross chamber filling.

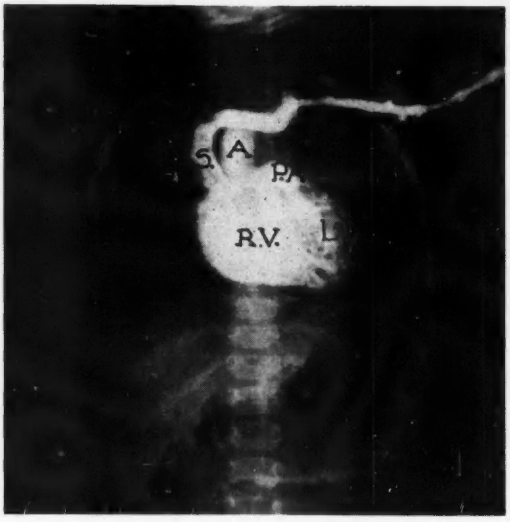

Figure 3.—(b) Antero-posterior cardiogram of same patient as Figure 3(a). The aorta is descending on the right side. The aorta fills at the same time as the pulmonary arteries. The left ventricle remains relatively empty.

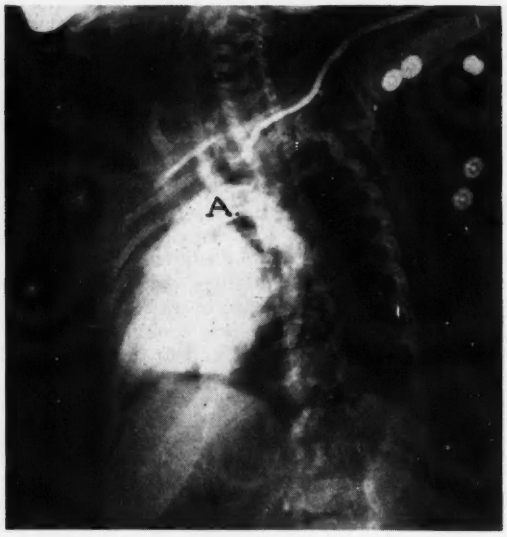

Figure 4.—The pulmonary arteries are not visualized. Necropsy showed complete atresia of the pulmonary artery at its origin. The flooding of the entire heart with diodrast resulted from the presence of an interventricular septal defect and a single, common ventricle. The diodrast cardiogram is of the heart of patient 2, Table III.

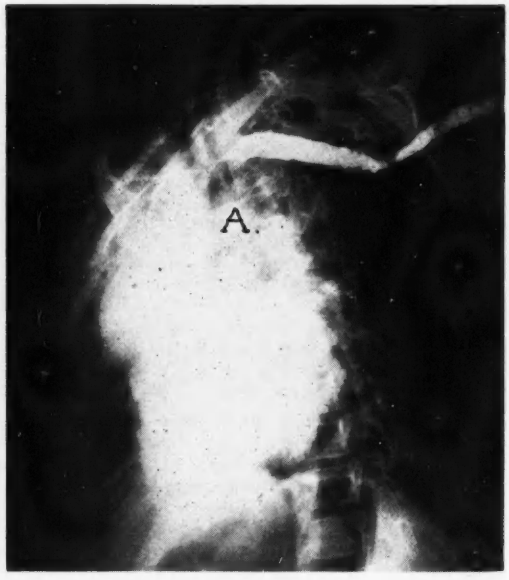

Figure 5.—Pulmonary arteries poorly shown. There is overriding of the aorta. (This latter vessel fills at the same time as the pulmonary arteries.) There is marked cross chamber filling yet this patient was greatly improved by the Blalock operation.

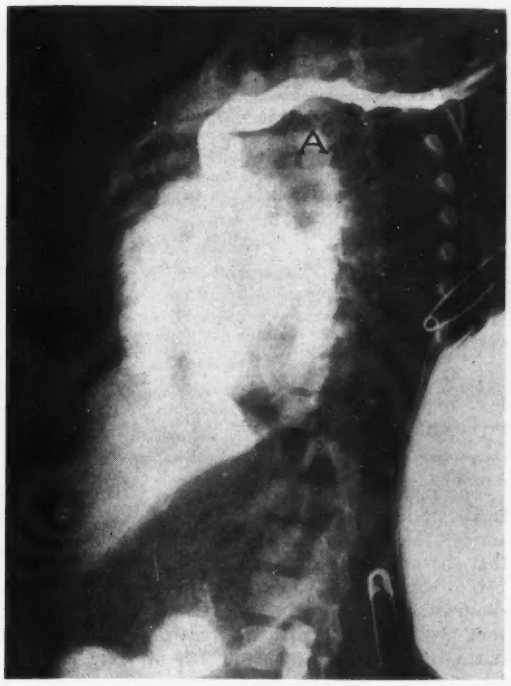

Figure 6.—There appears to be overriding of the aorta. The pulmonary arteries are poorly shown, yet the pressure in the right pulmonary artery in this patient was 760 mm. of water and no shunt operation was carried out.

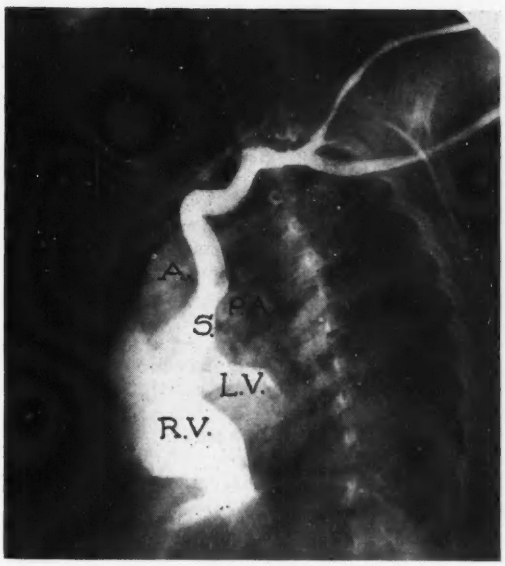

Figure 7.—Diodrast cardiogram of Case 1, Table III (drawing of heart and great vessels shown in Figure 1.) All of the blood leaving the right heart is carried by the aorta. The pulmonary arteries are supplied by the anomalous vessel from the descending aorta (probably an enlarged bronchial artery).

vessels that arise from the aortic arch were utilized. The carotid vessels were employed too frequently but as we have accumulated operative experience we rarely use any vessel other than the subclavian artery. Blalock emphasizes the importance of not interfering with the cerebral blood supply whenever it is technically possible.

TABLE IV.—*Vessels Utilized*

Right innominate	1
Right carotid	5
Right subclavian	5
Left carotid	2
Left subclavian	8
Division of both left subclavian and left carotid	1

Additional measurements of the pressure within the pulmonary artery (mm. of saline) and the width of the pulmonary artery are given in Table V. Figure 8 shows very well how the pulmonary artery may be large in caliber yet the amount of blood transported to the lungs be insufficient because of a stenosis proximal to the pulmonic valve.

TABLE V.—*Measurement of Pulmonary Artery*

Age	Pressure	Diameter
30 years	190 mm.	15 mm.
7¾ years		10 mm.
3 years		10 mm.
4 years		10 mm.
17 months		8 mm.
20 months		7 mm.
11 years	20 mm.	15 mm.

Table VI shows the total number of deaths in this group of patients. These figures compare favorably with those presented by Dr. Blalock.

TABLE VI.—*Mortalities*

	Total Deaths
22 Patients receiving shunt	1
6 Patients receiving no shunt	3
	4 (14+%)
Anastomosed group	4.5%

The postoperative complications are listed in Table VII. The only permanent complication was probable complete paralysis of the recurrent nerve (unilateral, on the operative side) in two patients. This complication occurred in the male aged 30 and indicates the difficulty of the dissection in the older age group, particularly in the freeing of the subclavian artery distally to the branching of this vessel.

Chylus thorax appeared in a boy of 2½ years of age, in whose case the approach had been right sided. Several taps were required but finally the fluid was completely absorbed one month following operation with no other treatment than the chest aspirations.

The numbness in the hand on the side on which operation was done occurred in the 30-year-old patient. Although annoying, this symptom is not

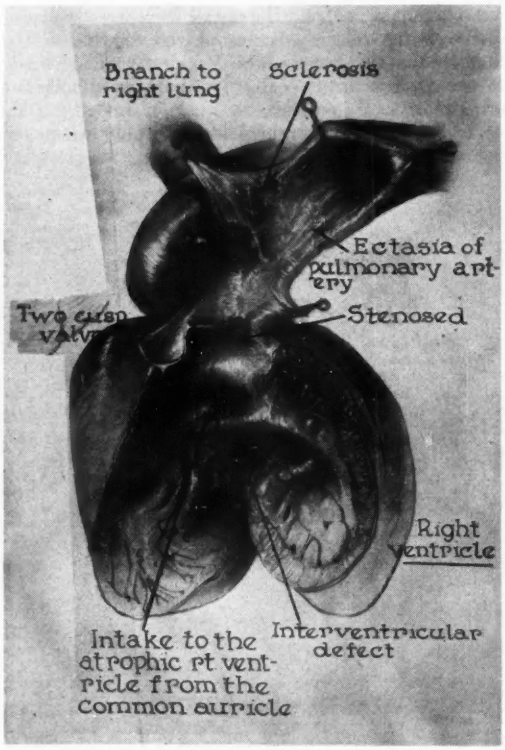

Figure 8.—This drawing is from a necropsy specimen. Note the marked ectasia of the pulmonary artery distal to the atresia. A large pulmonary artery in the diodrast cardiogram does not necessarily contraindicate the Blalock operation.

TABLE VII.—*Postoperative Complications*

Permanent hoarseness	2
Postoperative intrapleural bleeding (Spontaneous cure after 5 days)	1
Horner's syndrome (Both disappeared before leaving hospital)	2
Numbness in hand on operative side	1
Chylous thorax	1
Cranial irritation (Twitching of hands)	1

(17-month-old female, 2nd postoperative day, relieved by removal of 120 cc. of blood from left femoral vein.)

disabling and probably is the result of division of the subclavian artery.

The cranial irritation that occurred in one patient was immediately relieved by the withdrawal of 120 cc. of blood after a cut down on the common femoral vein. Hydration is carefully watched in all these patients; fluids are given by mouth until four hours before the operation. Normal saline solution is administered intravenously by slow drip during the operation. Fluids are continued parenterally during the immediate postoperative period until the patient is able to take by mouth at least 1500 cc. daily (young age group).

Table VIII outlines the number of instances of right sided aorta and the results in the 22 cases receiving the shunt.

TABLE VIII

Right Sided Arch		
Total cases having right sided aorta		9*
Cases in which x-ray failed to establish diagnosis (or was of no help)		2
Results in 22 Cases Receiving Shunt		
Deaths		1
Continuous audible murmur present		16
Excellent result	14	
Good result	2	
Continuous audible murmur not present		5
Excellent result	1	
Good result	1	
Fair result	2	
Poor result	1	

* All 9 cases received shunt operation.

The incidence of right sided arch is higher than in Dr. Blalock's larger series (one in five in Blalock's series). The x-ray department could not be certain that the aorta was descending on the right side in two of these nine cases. We now know that the diodrast cardiogram in the antero-postero projection will unequivocally demonstrate whether the aorta is descending upon the left or right side of the thorax.

The one death occurring in the group that received the shunt operation was that of a female 4¾ years of age. The heart stopped three times during the operation but the anastomosis between the right common carotid and the right pulmonary artery was accomplished. The patient expired a few hours after surgery. Necropsy revealed a pronounced infundibular pulmonic stenosis. Had the patient survived, she should have received considerable benefit from the operation.

A continuous murmur is audible in 16 of the 21 patients who have survived the Blalock procedure. When last examined a continuous murmur could not be elicited in five patients. The results are all excellent or good in those cases where a continuous murmur is audible. It would appear some blood is passing through the shunt in four of the five patients that do not have a continuous murmur since there has been some improvement in four. The patient classified as a poor result is the 17-month female who suffered from cerebral irritation during the postoperative period and was greatly improved by the removal of blood from the femoral vein. We intend to reoperate upon this patient, this next time on the contralateral side and probably anastomose the aorta to the left pulmonary artery.

Figures have not been presented to show the marked reduction in red blood count, hemoglobin and hematocrit that follows the Blalock operation. Reduction in these determinations is constant when the operation is successful and the anomaly corrected is a true pulmonic stenosis. We have observed the red blood cell count drop from 8.9 million to

4.67 million (per cmm. of blood) in six days following the shunt operation. (This particular patient lost very little blood at the time of surgery or during the postoperative period.)

SUMMARY

The purpose of this communication has been to present the results in 28 patients who have undergone exploratory thoracotomy with the intention of performing the Blalock operation if feasible.

The gratitude of both patient and parents that follows the successful completion of the Blalock operation has been a great thrill and stimulus to those of us who have treated the patients embodied in this report. The Department of Anesthesia at the University of California Hospital has played an important role in the successful completion of operations already presented.

The contribution of Dr. Alfred Blalock and Dr. Helen Taussig has been justly accredited by the leaders of our profession throughout our country. The greatness of the contribution of these two doctors can possibly be better expressed by the following words written by the mother of a child who has had the benefit of Blalock and Taussig's contribution: "There are no words to express our feelings of gratitude and happiness for making it possible for our little boy to be well and happy and able to play as other children."

REFERENCES

1. Blalock, A., and Taussig, H. B.: Surgical treatment of malformations of the heart, J.A.M.A., 128:189 (May 19), 1945.

2. Blalock, A.: Physiopathology and surgical treatment of congenital cardiovascular defects, Bull. New York Acad. of Med., 22:57, 1946 (Harvey Lecture).

3. Blalock, A.: The surgical treatment of congenital pulmonic stenosis, Annals of Surgery, 124:879-887 (November), 1946.

4. Blalock, A.: The use of shunt or by-pass operations in the treatment of certain circulatory disorders, including portal hypertension and pulmonic stenosis, Annals of Surgery, 125:129-141 (February), 1947.

5. Potts, W. J., Smith, S., and Gibson, S.: Anastomosis of aorta to pulmonary artery, J.A.M.A., 132:627 (November 16), 1946.

Simplified Intestinal Intubation with Miller-Abbott Tube

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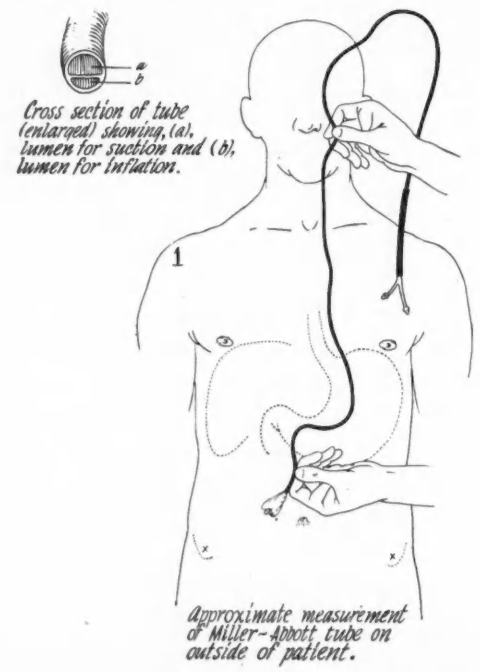
THERE is still a lack of standardization in methods of intestinal intubation with the Miller-Abbott tube. The following steps and use of an outside balloon on the inflation portion of the tube have served to simplify this procedure:

1. Test the balloon for leakage and capacity and measure roughly the distance from nose to pylorus on the outside of the body. (Figure 1.)
2. Insert the tube into the stomach. Immobilize the tube by taping it to the upper lip, allowing several inches of slack in stomach. (The markings will be between the 75 centimeter and one foot mark on the tube at the nose.)
3. Insert 10-15 cc. of water and 4-5 cc. of air into the balloon in the stomach and attach a second balloon to the outside inflation end of the tube. Elevate the patient's trunk and head slightly and encourage him to lie on the right side for intervals. Also, ask the patient to think about his favorite foods in an effort to excite psychic digestion. (Figure 2.)
4. In cases of obstruction, suction is started. In preoperative cases where the tube is being installed prior to right colectomy procedures, a nonresidue diet is continued without suction.
5. When the balloon in the stomach passes into the pylorus or duodenum, the water in the inside balloon is displaced through the inflation portion of the tube and will be observed in the outside balloon. If suction is being used, bile colored material will be seen in the suction bottle. The metal bucket's position may be checked by x-ray examination. (Figure 3.)
6. The distal end of the tube is proven by the above evidence to be in the duodenum. Then, by gentle squeezing of the outside balloon, the water is dis-

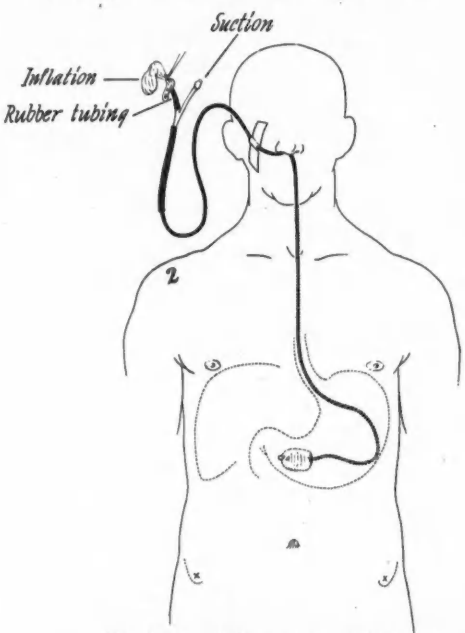
†From the Section of Bowel Surgery, Hollywood Presbyterian Hospital, Los Angeles.



Cross section of tube (enlarged) showing, (a), lumen for suction and (b), lumen for inflation.

Approximate measurement of Miller-Abbott tube on outside of patient.

Figure 1



Tube in place before engagement by pylorus. Distal balloon inflated, proximal balloon being attached to inflation outlet of tube.

Figure 2

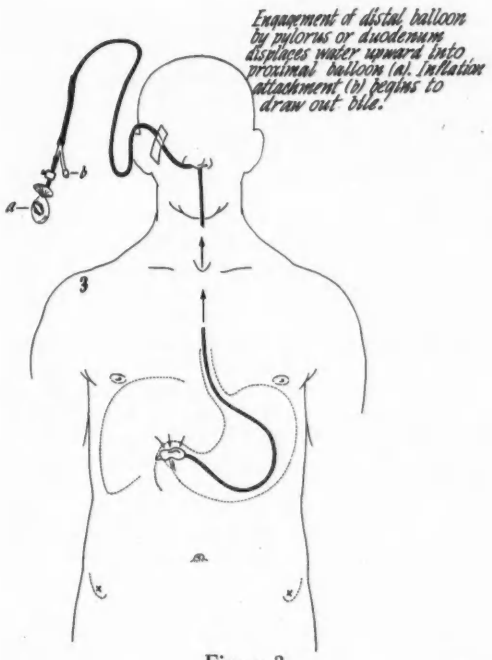


Figure 3

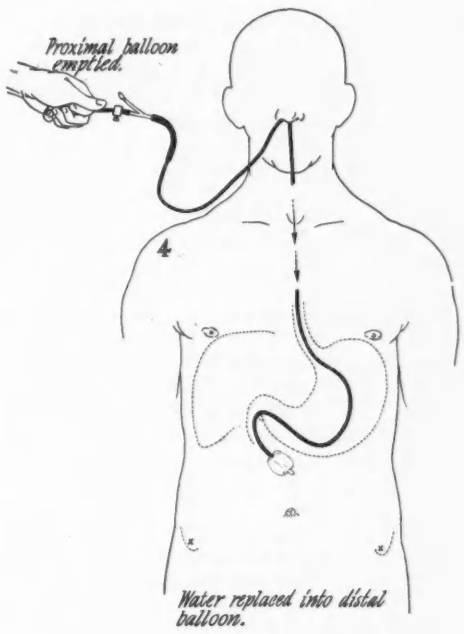


Figure 4

placed from the outside to the inside balloon. A clamp is placed on the inflation tube to keep the water in the inside balloon. (Figure 4.) The tube is mobilized by removing the adhesive tape from the upper lip and is kept oiled at intervals with:

R Cocaine alkaloid .....¼ of 1%
Phenol .....¼ of 1%
Oil of rose water to scent, in light mineral oil from a dropper bottle.

7. When the tube has descended to the desired location in the bowel tract, the clamp on the inflation tube and the outside balloon are removed, and the water is sucked out of the inside balloon.

CONCLUSION

The above procedure has saved much time and obviated unnecessary discomfort for the patient. The danger of coiled slack tube tying itself into knots is removed. The simulated bolus of the inside balloon is removed when the tube has sought its desired depth by evacuating the water from the inside balloon. This is not possible when mercury and other heavy materials are used in the balloon.

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Anesthesia for the Chronic Poliomyelitis Patient

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THE writer administered anesthetics to 370 chronic or "old" poliomyelitis patients over a period of four years. These were almost all in cases in which operation was done by Harvey E. Billig, M.D., of Pasadena, California, in his research work on nerve regeneration, and they form the basis for this study. It is necessary to know something of Dr. Billig's surgical procedures to understand some of the anesthetist's difficulties and to explain some of his conclusions.

SURGICAL PROCEDURES

Surgical treatment of these cases has been divided into three phases. The first or purely surgical phase included 71 cases and consisted of cutting down to, exposing and interrupting the motor nerves by pinching them with a forceps. These operations were called "nerve motor axon interruptions" and they lasted from one to four hours, depending on the number of nerves to be pinched. The anesthesia in these cases was mainly cyclopropane and oxygen, with endotracheal for 11 of the longest cases.

The second phase was the so-called "manual manipulation." This phase included 195 cases. In this operation no incision was made but a blunt instrument resembling a cold-chisel with a handle was used. It indented the skin down into the paralyzed muscle, separating the fibers and thus stretching and crushing, or interrupting, the nerve fibrils. In this operation the patient is shaken severely and there is heavy pressure brought to bear when thorax, back or abdomen are worked on, all of which interferes with a smooth anesthetic. These operations took from 15 minutes to one hour. During this phase we did a lot of experimenting to find the ideal anesthetic, using the three gases and ether in various combinations, as well as pentothal, avertin and spinal.

The third and last phase, in which we are engaged at present, consists of 104 cases, 96 of whom received sodium pentothal anesthesia, and eight (small children) open drop ether. For these patients Dr. Billig has invented and is using a pneumatic drill which is run by compressed air, and an electrically vibrated drill, both with cold-chisel like points. These instruments vibrate at about 3,200 impulses per minute and are producing better results than instruments formerly used. The operations last from 15 to 45 minutes. The explosion hazard explains why pentothal is the anesthetic of choice.

Read before the Section on Anesthesiology at the 75th Annual Session of the California Medical Association, May 7-10, 1946, Los Angeles.

PREOPERATIVE EXAMINATION

A preliminary physical examination by the anesthetist is essential, because the poliomyelitis patient does not take an anesthetic well for these reasons:

1. He is flabby and weak muscled because of his enforced inactivity.

2. His heart muscle is flabby as evidenced by the fact that bradycardia under cyclopropane and oxygen anesthesia is not too common. In 131 of those anesthetized in the cases here under review, 76, or 58 per cent, ran an abnormally high pulse, ranging between 90 and 120 per minute. Also, in many cases the heart seemed to show signs of "petering out" earlier than normally might be expected, with the pulse increasing steadily in rate after an hour or so of anesthesia.

3. He may have weakened muscles of respiration as a result of his illness, or he may have scoliosis with twisting of the thorax on the abdomen, or his abdominal muscles may be seriously weakened so that the rib margins move in instead of out on inspiration. About one-third of our cases had noticeably weakened thoracic or abdominal muscles or both.

4. Most poliomyelitis patients, made introvert by the nature of their disease, are tense and sensitive.

Because of these abnormalities a majority of poliomyelitis patients may be considered only fair risks as far as anesthesia is concerned. The anesthetist should study the patient's blood pressure and heart action, the respiratory movements of the upper and lower thorax, the strength of abdominal muscles and the amount of malformation due to scoliosis and rotation of the chest.

PREMEDICATION

The next thing to consider is the premedication. Because the patient is flabby and his respiratory muscles probably weakened, the medication should be minimal. In our cases, the night before operation adults were given pentobarbital (nembutal) 100 mg., one and one-half hours before surgery a second capsule of pentobarbital 100 mg., and one hour before surgery a hypodermic of morphin 12 to 16 mg. combined with atropin 0.3 mg. to 0.4 mg. In only especially husky males is the pentobarbital increased to 194 mg. for sleep and before surgery. Scopolamine was not used because it "deepens the morphine narcosis," (Sollman). It deepens still further, while atropin stimulates, and these patients need stimulation. Again, to quote Sollman, scopolamine is mainly sedative in all doses, while moderate doses of atropine are excitant.

ENUMERATION OF TYPES OF ANESTHETICS

A total of 370 anesthetics were administered. Of these 132 were cyclopropane and oxygen, 37 were cyclopropane and ether, 28 were ethylene and ether with cyclopropane induction, four were nitrous oxide and ether with cyclopropane induction, and seven were ethylene and oxygen with cyclopropane induction—a total of 208 gas anesthetics. Of the remaining 162, 23 were spinals, 23 were open drop ether with ethyl chloride induction, three were avertin and gas, 111 were sodium pentothal intravenously, and two were mixed—that, is they took an excessive amount of pentothal so we switched to gas.

We limited ourselves to one full gram of pentothal, so if a patient took a gram in 10 to 15 minutes we changed to gas and oxygen.

CHOICE OF ANESTHETIC

The poliomyelitis patient looks like an ideal "set-up" for cyclopropane and oxygen, that is, a light cyclopropane with plenty of oxygen, and we used it in all our early cases. It worked well for the surgical "nerve motor axon interruption" operations where the procedure took a long time (from one to four hours) and where endotracheal administration was resorted to in 11 of the longer cases. But the after-results were not so pleasing. Sixty-three of 118 patients, or 53 per cent, developed excessive nausea and vomiting lasting four to twenty-four hours. This is unusual when compared with the normal run of surgical cases. We tried all sorts of ways to avoid it; we tried pantapon and also dilaudid instead of morphine; we tried intravenous glucose, adrenal cortex, all to no avail.

Then in the second phase when the "manual manipulation" was being done, with its shaking of the patient as in a violent massage, its turning of the patient from a supine to a prone position, its sudden changes in pain stimuli, the need for abdominal relaxation, and the changing pressures on the back and chest interfering with normal respiration, we found that cyclopropane and oxygen was not adequate. Stridors developed easily; cyanosis was frequent even with excessive oxygen; there was leakage of gas around the mask and a smooth anesthetic could not be maintained.

So we experimented with gas mixtures—cyclopropane and ethylene; cyclopropane and ether; cyclopropane, ethylene and ether; and finally ethylene or nitrous oxide and ether with cyclopropane induction. We found that the addition of ether to ethylene or nitrous oxide with cyclopropane induction made for a smoother anesthetic, and that stridor or laryngospasm was less frequent, the respirations were stronger and deeper, a good color was maintained throughout, and a loss of gas did not so suddenly affect the plane of anesthesia. Finally we found that postoperative nausea and vomiting was less, only 38 per cent, or 14 out of 37 cases, being so afflicted.

Our experience developed a few general observations on gas anesthesia for poliomyelitis patients:

1. An airway should not be used unless necessary, because the shaking of the patient also shakes and rattles the airway in the pharynx, which sets up a laryngospasm very easily.

2. When the back and chest muscles are worked on, especially at T6 and above, the gas is forced out of the patient's lungs sharply, and breath-holding or laryngospasm usually develops. Frequently the anesthetist has to ask the surgeon to pause for a minute or two until respiration can be re-established by bag pressure.

3. When a patient with paretic respiratory muscles is lying on his face, he must be helped by bag pressure to breath deeply enough to prevent cyanosis. Frequently he just is not strong enough to expand his lungs well against his own body weight.

As to the other anesthetics, we used avertin and gas three times only, because the shaking of the patient and the pressures on the abdomen when the abdominal muscles were worked on, forced the fluid out of the rectum. Open drop ether with ethylchloride induction was used on 23 small children under six years of age and on two adults who took gas poorly. It worked smoothly. Twenty-three spinal anesthetics were given to those who asked for them. Dr. Billig made careful muscle tests of these patients afterward and found that no damage had been done. However, there are two reasons for not recommending this type of anesthetic in manipulative surgery. First is that, because of the light premedication, the patients are only one plus drowsy (on a scale of 1 to 4 plus) and the shaking makes them quite uncomfortable. Second, in our experience there has been an abnormally high incidence of spinal headache, four out of twenty-three having complained of it the next day. It is probable that some of the patients had headaches of which we heard nothing because usually they are discharged the day after surgery, or about 30 hours postoperatively. However, there appears to be no reason why a spinal should not be used on any poliomyelitis case for general surgical procedures in the lower abdomen or lower extremities.

PENTOTHAL SODIUM

Pentothal sodium intravenously was used 111 times in this series, the first 26 being in the second or "manual manipulation" phase. We did not like it too well in this procedure because the shaking of the patient occasionally dislodged the needle. Moreover, when the patient was moved from his back to his abdomen we removed the needle and then had to reinsert it in a difficult position. Another reason for our initial unsatisfactory experience was that, knowing of its respiratory depressing effects we gave too little pentothal to relax the abdominal muscles.

In the third phase, or pneumatic drill operation, however, we have used pentothal almost exclusively (except for eight ether anesthetics on small children) with good results. Experience with 85 cases thus far has taught us to give sufficient pentothal to bring

about moderate abdominal relaxation. Also we have learned to press the needle well into the vein so that it is not easily dislodged; and when the patient is turned over from back to abdomen we strap the needle in place with adhesive tape and remove only the syringe. To protect the patient a gas machine is always at hand to furnish oxygen if needed. We have it in readiness in every case in which the chest or back is to be worked on, and oxygen is given if there is any color change such as pallor or slight cyanosis. We have used oxygen or oxygen and nitrous oxide in 20 of 111 cases.

There have been some interesting complications with pentothal. Fifteen cases exhibited trembling or shaking which might be classified as a mild type of convulsion. This occurred when the anesthesia was light, and disappeared when it was deepened. Patients who trembled when being induced trembled again during recovery in bed. (The nurse in charge should be warned of this, lest she think the patient is having a chill.)

Eleven cases exhibited signs of early shock, with loss of color or pallor, but only two showed signs of moderate shock with a rapid and weak pulse needing treatment with trendelenberg position, caffein or coramine.

There were two bizarre reactions. One patient's face became yellowish, but his pulse was 84 and respiration 18 and there was no other sign of trouble. Another patient had a greyish pallor and a hyperpnea, with respiration rate going up to 50 per minute whenever the pentothal was pushed. Neither reaction is explainable.

The advantages of pentothal sodium are these: It is safe to use in the presence of sparking apparatus such as the electric drill; it is easily administered; the patients prefer it to any other anesthetic because it seems to be nothing but another hypo and has pleasant after-effects. Vomiting is negligible, although 20 of the 111 (or 18 per cent) experienced it in some degree. Fourteen vomited once, four more than once though moderately, and two severely and over a period of several hours.

COMPLICATIONS AND SEQUELLAE

Although considerable shock might be expected to develop during operations such as those reviewed here, because of the muscle trauma, the fact is that it occurred rather rarely in the 370 cases. Of the 370 cases, four (1 per cent) required intravenous glucose during the operation, eight (2 per cent) required intravenous fluids afterward and 19 (5 per cent) required carbogen inhalations with coramine or caffein postoperatively—a total of 31, or 8 per cent, showing sufficient signs of shock to require treatment. It is interesting to compare this 8 per cent for the entire series with the experience in the 111 cases in which anesthesia was by pentothal. In the pentothal series, only 2 per cent required treatment for shock.

As to other complications, there were four spinal headaches, one case of hiccoughs, and one pulmonary complication—a dry cough following endotrachael anesthesia. No pentothal sensitivity was encountered.

In general these patients were in good condition the next day, ate a good breakfast and were discharged at noon. Few complained of muscle soreness or other disability.

CONCLUSIONS

1. Because the poliomyelitis patient is not physically a normal person, he should be examined carefully before operation.
2. Light premedication should be the rule.
3. If a gas anesthetic is to be used, it should be of a respiratory-stimulating type. Adding ether to cyclopropane is good, but in our experience the best is ethylene and ether with cyclopropane induction.
4. Spinal anesthesia is safe for operations below the umbilicus.
5. Sodium pentothal intravenously, with oxygen by mask if necessary, gives good anesthesia and is the anesthetic preferred by the patient.

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REFERENCES

1. Billig, H. E., Jr.: Muscle reinnervation, J. Internat. Coll. Surgeons, 7:457-461 (Nov.-Dec.), 1944.

2. Billig, H. E., Jr., and van Harreveld, A.: New aspect of muscle reinnervation, U. S. Nav. Bull., 41:410-414 (Mar.), 1943.

3. McFarland, J. W., Billig, H. E., Jr.: Taylor, G., and Dail, C. W.: Kenny treatment combined with neurotripsy in care of poliomyelitis, Arch. Phys. Therapy, 25:645-650 (Nov.), 1944.

4. Sollman, T.: A manual of pharmacology, Philadelphia, W. B. Saunders Co., 1932, Ed. 4, pages 397 and 399.

The Use of Antibiotics in Surgical Practice*

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THE usefulness of antibiotic materials in the therapy of infections is well known. New preparations are being developed, and the scope of application of antibiotics now available is being extended. At the same time, however, that the efficacy of certain of these materials is becoming established, the limitations of their usefulness are likewise becoming apparent. In a consideration of the use of chemotherapeutic materials in surgical infections it must be remembered that these materials are merely adjuncts to surgical treatment. They do not replace sound surgical judgment and diligent observation of well-established surgical principles.

Antibiotics are substances derived from the metabolic products present in the culture media upon which are grown certain living organisms, particularly the molds. Of the scores of such substances prepared, only three have proved to be of clinical value by virtue of possession of the properties of high bacterio-static and bactericidal potency, relative stability, and low toxicity. These are penicillin, tyrothricin, and streptomycin. Tyrothricin does not warrant lengthy consideration in this discussion. It was first prepared by Dubos in 1939 from Bacillus brevis, and was found to be made up of two constituents, gramicidin and tyrocidine. It is particularly effective against gram-positive organisms, but its marked toxicity limits its usefulness to local application, in the form of ointments and compresses, to surface lesions. Given intravenously in experimental animals, the material causes hemolysis of the red cells, destruction of the leucocytes, liver necrosis, and death. Given intramuscularly or subcutaneously, it produces a local sterile tissue necrosis and loses its effectiveness. Its usefulness is restricted to lesions that are open, with adequate surgical drainage, where there is sufficient blood supply, and in which the predominant organisms are streptococci or staphylococci, or both.[14]

PHYSICAL, ANTIBACTERIAL, AND PHARMACOLOGICAL PROPERTIES

Penicillin, first discovered by Fleming in 1929 and then applied clinically by Florey in 1940, is produced by the mold Penicillium notatum and is the most useful of the antibiotic agents. It possesses the stability, the low toxicity, and the effectiveness against certain bacteria required of a practical antibiotic. The unit of penicillin is the amount which, when added to 1 cc. of a broth culture of a standard strain of staphylococcus, will just inhibit growth of the organism. Manufacturers produce purified sodium salts of penicillin for the usual parental use, calcium salts of penicillin for local use, and, recently, potassium salts of it for use in a beeswax and oil preparation.

An investigation of the increased relapse rate in cases of syphilis treated with supposedly adequate doses of penicillin revealed the existence of the four major fractions G, X, F, K, whose production is dependent upon the conditions under which the antibiotic is produced from the mold. Regardless of *in vitro* activity, in the body, penicillin G and X are much more effective against infection than K and F,[2,7] and attempts are made now to produce commercial penicillin with as high as possible a proportion of penicillin G. Although penicillin X is more active than G against a few organisms, penicillin G has the greater potency against most organisms and against the spirochete of syphilis. Synthetic crystalline penicillin G, known as benyzl penicillin, has recently been produced at Cornell University.[6]

The production of streptomycin by the mold Actinomyces griseus was described by Waksman[25] of New Jersey in 1944. It was subjected to strict scrutiny, as had been penicillin, and it also was found to possess the properties of stability, low toxicity, and effectiveness against a variety of pathogenic organisms which in this instance were principally the gram-negative bacilli. Streptomycin salts (hydrochloride and sulfate) are dispensed as a light yellow powder in the dry state in vials containing 1.0 gram, 0.5 gram or 0.25 gram. One gram contains 1,000,000 units. The unit is defined in a manner similar to that of penicillin except that the standard organism is Escherichia coli. Against an organism susceptible to both penicillin and streptomycin, the unit of penicillin is 10 to 15 times as effective as the unit of streptomycin, so that in general, where the average daily dose of penicillin is perhaps 200,000 to 300,000 units, that of streptomycin is 2 to 3 million units.

Before the indications for use, the proper dosage, and the mode of administration of penicillin and streptomycin could be determined, it was necessary to have an understanding of the antibacterial properties, the absorption, excretion, distribution, and toxicity of these substances.

It is relatively simple to determine sensitivity of organisms to antibiotics in the test tube. Unfortunately the determination of *in vivo* sensitivity is not possible. There seems to be an enormous discrepancy, particularly with streptomycin, between the sensitivity of organisms *in vitro* and the effect of streptomycin on these same organisms in the body.

In general the organisms usually considered "sensitive" to penicillin are the gram-positive cocci such as the streptococcus, the staphylococcus, and the pneumococcus; and the gram-positive bacilli of anthrax, diphtheria, botulism, tetanus, and gas in-

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fection. In addition, penicillin inhibits the gram-negative meningococcus and gonococcus. There is no organism that shows an *absolute* resistance to penicillin in sufficient concentration. Organisms which are usually classified as "sensitive" are those inhibited by concentrations of penicillin of 0.1 unit per cc. or less, which is a concentration fairly readily obtainable in the body.[5] Some organisms that are usually considered resistant are inhibited by concentrations of 1 to 3 units, or as high as 10 to 300 units per cc., which are concentrations that can be obtained clinically in the urine. It must be emphasized, however, that under clinical conditions higher concentrations may be required than are indicated by *in vitro* tests, as the number of organisms may be higher and inhibitory substances such as penicillinase, and undoubtedly others as yet undiscovered, may be present.

The organisms commonly considered to be sensitive to streptomycin are those whose growth *in vitro* is inhibited in a concentration of 8 to 16 units per cc. This concentration can be obtained clinically in the serum and most body fluids. In certain instances, however, one is not limited to the treatment of organisms with this high sensitivity. In the urine, concentrations of 500 to 1000 units of streptomycin per cc. are easily attainable. The streptomycin-sensitive organisms include the gram-negative bacilli, Escherichia coli, Bacillus aerogenes, Bacillus proteus, Bacillus pyocyaneus, the typhoid-paratyphoid group, Friedlander's bacillus, Hemophilus influenzae, Bacillus pertussis, Brucella abortus, and the organism of tularemia. Streptococcus fecalis and the tubercle bacillus are also included.

It is not an uncommon occurrence to have infections fail to respond to penicillin or streptomycin even though the organisms are definitely susceptible at the onset of treatment. Further sensitivity tests in many such instances show an enormous increase in resistance to the antibiotic. These highly resistant organisms are thought to be either the overgrowth of a few non-sensitive organisms not discovered before treatment, or the result of an actual increase in resistance of the insufficiently-treated, previously highly sensitive organisms. It seems likely that the correct explanation is that of an acquired resistance in organisms originally sensitive but exposed to insufficient concentrations of the drug. This argues for heavy doses of the antibiotic that will be adequate from the very start of treatment. Of great importance in therapy is the delivery of adequate amounts of the antibiotic to the actual site of infection, so that each organism may be bathed in a lethal concentration maintained sufficiently long to allow the natural defenses of the body to deal with these devitalized bacteria.

Penicillin given parenterally distributes itself rapidly throughout the body, so that in 15 to 20 minutes after intramuscular injection it reaches a maximum concentration in the blood stream. However, since it is rapidly eliminated, largely by the kidneys, only traces remain in the blood stream two hours after a single dose. The material does not pass through the meninges or into the pleural or joint cavities, making local injection of penicillin necessary in infections of these spaces.

The ordinary penicillin given *orally* in the usual doses does not produce a therapeutic level in the blood stream. Of the three possible explanations, namely, destruction by gastric juice, failure of absorption, and inactivation by colon bacteria, recent experimental evidence points to failure of absorption as the difficulty.[23,24] The duodenum is felt to be the location of maximum absorption. Under investigation are agents which will convoy the penicillin through the duodenum, but release it before it can be carried to the colon.

Streptomycin also distributes itself generally throughout the body with the exception of the thecal and pleural spaces. About 80 per cent is excreted through the kidneys in 24 hours but its excretion is much slower than that of penicillin.[10] This allows a higher concentration of the drug to be built up in the blood stream with smaller and less frequent doses. Almost 100 per cent of streptomycin taken orally appears in the stool in the active form. The drug does not seem to pass in either direction through the bowel wall. In bile, penicillin appears in the same concentration as exists in the blood stream. Streptomycin appears in the bile in about half the blood stream concentration.

METHODS OF ADMINISTRATION

Originally, penicillin dissolved in saline solution was given by intermittent or continuous parenteral administration. Newer methods of administration are being developed along two lines: the first is designed to promote slower absorption or decrease the rate of elimination in an effort to decrease the number of injections necessary to maintain a satisfactory blood level, and the second to apply high concentrations of penicillin topically to the site of the infection. The most practical slow-absorption method is the use of the preparation that has become known as the "Romansky" formula. This consists of 300,000 units of amorphous calcium or crystalline potassium penicillin in 4.8 per cent beeswax in peanut oil totalling 1 cc. Studies made by Romansky,[21] and repeated by others, show that the maximum concentration of penicillin in the blood occurs four hours after one such injection and is about 0.6 unit per cc., declining gradually to 0.06 units per cc. 12 hours after injection. At present it seems that to achieve therapeutic levels with certainty, one should administer the beeswax and oil preparation every 12 hours. The injection produces a temporary local soreness, but no muscle necrosis. The beeswax is removed by phagocytosis and disappears by the 30th day. It is important that the material be injected intramuscularly. Of 4,000 cases reported by Romansky, sterile abscess occurred in only two, in both of which the injection was subcutaneous. The therapeutic results in these 4,000 cases were satisfactory and in all ways comparable to those obtained by the usual penicillin-in-saline, frequent-injection method. The incidence

of allergic reactions with the Romansky preparation was 5 per cent.

It has been demonstrated that when penicillin is given by mouth, in order to produce comparable concentrations in the blood stream, there is required a dose five times as large as when the drug is injected parenterally. Many attempts have been made to increase the passage of penicillin from the gastrointestinal tract into the blood stream. These include dissolving the penicillin in such materials as peanut oil, sesame oil, or cocoa butter; encasing the penicillin in hardened gelatin capsules or resin cellulose plastic capsules; and administering the penicillin orally with antacids such as sodium citrate or aluminum hydroxide. A recent report[16] on five commercial preparations of penicillin for oral administration revealed that when doses of 100,000 units were given, barely adequate blood stream levels of 0.03 unit per cc. were attained by four of the substances in one-half to one hour and maintained only two hours. The conflicting results reported, the uncertainty of absorption, and the large amount of penicillin necessary to produce adequate blood levels, have prevented extensive use of oral administration of penicillin.

Penicillin administered by inhalation, or "aerosol" penicillin, is becoming popular in the treatment of respiratory infections.[11] Penicillin so used is easy to give, is less costly to administer, is deposited locally in intimate contact with infecting organisms on the bronchopulmonary mucosa, and is rapidly absorbed into the blood stream through the alveolar surfaces. Administered by inhalation, 50,000 units of penicillin produce blood concentrations of 0.05 to 0.20 units per cc. The crystalline sodium salt of penicillin is the least irritating and most commonly used. The usual dose is 50,000 units in 1 cc. of normal saline used as a spray at three-hour intervals with an ordinary rubber bulb hand nebulizer. Clinical results are encouraging, particularly in the acute and subacute infections. Favorable clinical effects noted are diminution of sputum, a change to a mucoid type of sputum, decrease in cough, and subsidence of signs of acute toxemia. Penicillin-sensitive pathogens are entirely eliminated from the sputum. Penicillin spray is particularly useful as a preoperative measure prior to lobectomy or pneumonectomy for bronchiectasis.

Local or regional injection of penicillin into an area of cellulitis or into the tissue immediately about a furuncle, carbuncle, or felon has been reported to yield good results[22] and to eliminate the need for systemic therapy. It would seem advisable to approach such therapy with a certain degree of caution in other than small, well-localized infections. The dosage recommended is 50,000 to 100,000 units in 2 to 10 cc. of saline injected directly into the lesion through several needles.

The sublingual oral administration of penicillin[9] has been reported to produce therapeutic blood levels, but this route of administration is not yet to be recommended in any but trivial infections because of the uncertainty of absorption.

Penicillin ointment, 500 units per cc. of lanolin or petroleum base, is widely and effectively used in superficial skin infections and ocular infections.

Streptomycin may be administered in the same manner as penicillin, but there are as yet insufficient clinical observations to warrant its administration in serious infections by routes other than intramuscular or intrathecal injection. Most serious systemic infections call for a daily dosage of 3 to 5 gm. dissolved in 2 or 3 cc. of saline, given in divided doses at four-hour intervals. Intrathecal administration is used in meningitis of Hemophilus influenzae where 50 to 100 mg. in isotonic saline solution are given intraspinally once or twice daily. It is important to start therapy with *adequate* doses to prevent an increase in resistance of the organism to the antibiotic. The place of oral administration of streptomycin in therapeutics is not yet determined. Doses of about 3 gm. daily given in six divided doses in water definitely have a bacteriostatic effect on the flora of the stool.

CLINICAL USES

It is not possible to deal here with the method of therapy and dosage scheme recommended in treatment of each of the infections that might be encountered in surgical practice. An understanding of the applicability of antibiotics and of the limitations of antibiotic therapy in surgical infections calls for an understanding of the fundamental difference between surgical and medical infections. These differences that make surgical infections less likely to respond to drug therapy have been well outlined by Meleney.[17] Surgical infections are characterized by a local spontaneous or traumatic breakdown of tissue, or localized exudation into a body cavity or into the substance of solid tissues. This necrotic tissue must be evacuated or absorbed in the healing process. The blood vessels in the wall of an abscess are thrombosed and any medication coming via the blood stream may have difficulty penetrating or diffusing into the focus far enough to reach the offending organisms. On the other hand, in a well localized lesion, opportunity is afforded for local application of medication. Many of the surgical infections are mixed infections where there may be synergistic action between bacteria and where one or more of the organisms may be resistant or actually antagonistic to the antibiotic. However, in the early stages of many surgical infections, before there is a breakdown of tissue there is a stage of diffuse inflammation or diffuse cellulitis. Drugs given at this stage or in infections of this type do not encounter the difficulties mentioned above and have a more favorable opportunity to contact and control any susceptible organisms.

It is thus seen, as Meleney has pointed out, that the factors that tend to limit the usefulness of antibiotic therapy include: (1) infection with organisms of low susceptibility, (2) presence of antagonistic substances such as penicillinase, (3) development of

resistance during therapy, (4) administration of inadequate doses, and (5) certain local characteristics of surgical infections preventing adequate contact of the drug with the organism and making necessary surgical treatment in the nature of drainage.

Time permits only a general discussion of the various clinical infections treated with antibiotic materials. From the accumulated experience with the use of penicillin in established surgical infections a few generalizations have been made:[17] (1) Penicillin alone or as an aid to surgery will control about two-thirds of the established surgical infections usually encountered. (2) Studies of the Committee on Chemotherapy of the National Research Council showed penicillin to be most effective in cases of furuncle, cellulitis, mastoiditis, carbuncle, suppurative arthritis, lung abscess, superficial abscess, brain abscess, and osteomyelitis. (3) Penicillin was found to be moderately successful in cases of deep abscess, thrombophlebitis, sinusitis, infected soft tissue wound, infected operative wound, otitis media, infected compound fracture, and ulcer of the skin. (4) It was found to be not so successful in cases of empyema, infected burns, gas gangrene, actinomycosis, peritoneal abscess, and diffuse peritonitis. (5) Penicillin therapy is more successful in acute rather than in chronic infections, and if given early rather than late in the disease. (6) Many cases of well localized surgical infection can be successfully treated with local injection of penicillin solution or local application of penicillin in ointment form. (7) Penicillin is not as successful in mixed infections as in those caused by a pure culture of a susceptible organism. (8) Important causes of failure include resistant strains of staphylococci or streptococci, mixed infections with organisms capable of producing penicillinase, too little or too late administration of penicillin, associated diabetes or arteriosclerosis, and too conservative surgery.

Fortunately, most of the penicillinase-producing organisms seem to be relatively non-pathogenic and are non-invasive so that local application of agents inhibiting their activity may permit penicillin to function at the site of the infection, be it given systemically or locally. Such agents are being investigated. One of these is streptomycin in concentrations of 500 to 5000 units per cc.

Penicillin has had a great effect on the recovery rate from septicemia due to staphylococci, streptococci, and pneumococci, which is usually associated with some other pathological process such as cellulitis, carbuncle, abscess, septic abortion, osteomyelitis, and so on. Such patients should receive intensive penicillin therapy parenterally, with intermittent intramuscular injections of perhaps 50,000 to 100,000 units of penicillin every three hours day and night. Such therapy should be continued for several days after the temperature has returned to normal and all clinical signs of active infection have disappeared. It is inadvisable to lessen the dosage during the therapy since this may lead to production and survival of penicillin-resistant strains of the infecting organism.

In the treatment of infected wounds, penicillin has been of great help in combating sensitive organisms, but of great importance here is the observation of the principles of adequate debridement, sufficient drainage, elimination of dead space, and suturing without tension. The drug should be administered parenterally to prevent further invasion of the infection. Benefit may be obtained from local application of the drug by means of irrigation, compress, or continuous instillation. Penicillin administration in cases of gas gangrene does not replace adequate surgical and antitoxin treatment, but it is a worth-while addition to the treatment of so serious a condition. Conflicting opinions exist regarding the value of penicillin in the treatment of tetanus. The consensus of opinion is that it should be given, but the usual measures should not be interfered with by antibiotic therapy.

One of the most frequently encountered serious infections in general surgical practice is peritonitis of intestinal origin. This is a complex process. It is practically always a mixed flora infection with streptococci, clostridia, and gram-negative organisms. Which of the organisms are the true pathogens is not certain. Very likely the gram-negative bacilli play a minor role. Furthermore, the role of the peritoneum is not entirely understood. Recent clinical experience[3] and experimental work[3] show that penicillin administered intramuscularly in frequent large doses in the order of 100,000 units every two hours is very effective in the control of peritonitis and is the best chemotherapeutic agent in use at the present time. It is thought that large doses in excess of the amount inactivated by the penicillinase formed as a result of the infection, overcome the sensitive, more pathogenic coccal and clostridial organisms, and allow the peritoneum to handle the less pathogenic gram-negative organisms. Since penicillin is effective in the presence of exudate and debris, it is worth while in generalized peritonitis from a perforated appendix to leave large amounts, such as 200,000 units in 50 cc. of saline, in the peritoneal cavity at the time of operation.

In pulmonary infections with sensitive organisms penicillin is beneficial. Daily local injection into empyema cavities together with parenteral therapy gives favorable results in from 30 to 40 per cent of cases. In acute putrid lung abscess, penicillin parenterally and by inhalation, together with general medical measures, has cured a high percentage of cases. In chronic abscess the value of penicillin lies in the reduction of the amount of infection before surgical treatment is undertaken. The same use is made of penicillin inhalations in cases of bronchiectasis to be subjected to surgical therapy.

In acute osteomyelitis the dramatic effect and unquestionable value of penicillin have been demonstrated again and again. The dosage must be large—40,000 to 50,000 units every three or four hours—and started early.

In chronic osteomyelitis the systemic and local, preoperative and postoperative use of penicillin have increased the percentage of successful seques-

trectomies, sinus closure operations, and bone grafting procedures. Truly, in this condition penicillin is an adjunct to surgical therapy and not a substitute for it.

The treatment of pyogenic abscess of the central nervous system has not changed materially since the advent of chemotherapy. The results in pneumococcic meningitis complicating fractures through the accessory sinuses have been exceptionally good. The drug is administered both parenterally and intrathecally.

In gynecological practice, penicillin has proved itself effective not only in the treatment of acute gonococcal disease and acute streptococcal infections, but also in the preoperative elimination of organisms in chronic inflammatory disease to be treated surgically.

In otorhinolaryngology cures of cavernous sinus thrombosis with penicillin are no longer rare. In this specialty, topical application of the agent finds widespread use in pharyngitis, tonsillitis, sinusitis, and otitis media, with generally favorable results.

Ophthalmologists make use of penicillin drops or ointment, in a concentration of 500 units per cc., in superficial infections about the conjunctiva. Infections of the eyeball are treated with parenteral injection since the drug readily enters the fluids of the eye that is inflamed. Beneficial results are reported by some who have injected penicillin directly into the eyeball.

Streptomycin has not yet proved as successful in gram-negative infections as penicillin in the gram-positive ones.[4,13,20,26] Mention should be made of the great efficacy of streptomycin in tularemia and Hemophilus influenza meningitis, but the results of its use in many surgical infections have been disappointing.

In the treatment of established wound infections in which the organisms are streptomycin-sensitive, the results have not been impressive whether this agent be administered systemically or topically. Thus, streptomycin is not appreciably different from other chemotherapeutic materials in management of wound infections. Adequate surgical treatment supplemented by systemic specific chemotherapy to control the invasive aspects of infection is still the chief therapeutic measure.

In bacteremia with sensitive gram-negative organisms the results with systemically administered streptomycin are good provided the focus of the infection can be eradicated whether it be an infected tooth, bone or renal carbuncle. The drug should be given intramuscularly in saline in a total daily dose of 3 to 5 gm. in eight divided doses of 3 to 5 cc. each.

In peritonitis of intestinal origin, streptomycin has not been remarkably effective. In one series[4] of 30 cases, 60 per cent were recorded as improved. The evaluation of any chemotherapeutic agent in an infection with so many variables is difficult. Investigation of streptomycin therapy in a more controllable experimental peritonitis in animals has shown it to have little effect. Penicillin definitely is the drug of choice in therapy of peritonitis.

Streptomycin is a useful agent in urinary infections produced by bacteria susceptible to the drug if they are not associated with obstruction, retention of residual urine, calculi, undrainable foci, or poor kidney function.[19] Any of the above factors acts to prevent all the organisms from coming in contact with a suitable concentration of the antibiotic. Such a situation favors the development of streptomycin-resistant strains of the organisms. Even though streptomycin is concentrated in the urine, the dose should be high—2 to 3 gm. daily in divided doses intramuscularly. If the infection does not yield in three or four days it is not likely that it will. It is desirable to determine whether or not the organisms are sensitive before subjecting the patient to the expense and discomfort of streptomycin therapy. About 60 per cent of properly selected cases of urinary infection show favorable results as evidenced by subsidence of clinical symptoms and sterilization of the urine. There are reports of cases of renal tuberculosis in which the urine has been cleared of tubercle bacilli by prolonged administration of streptomycin. It is not possible yet to say that the improvement will be permanent.

It has been demonstrated that streptomycin given orally in a dose of 1 gm. daily is more efficient than succinyl-sulfathiazole in reducing the stool bacterial count of Escherichia coli, Streptococcus fecalis and clostridium. As yet, however, no series of cases has been reported in which clinical or experimental results were noted with streptomycin used in the preparation of the large bowel for surgery. The preliminary work in this field is encouraging.

TOXICITY

The administration of penicillin has only rarely been attended by evidence of *severe* toxicity but reactions do occur. Those that are due to any direct toxic action on tissue itself are negligible. However, both commercial and crystalline penicillin possess definite antigenic and allergenic properties. Sensitivity to penicillin may be evidenced by immediate reactions usually occurring in patients with known penicillin sensitivity or previous exposure to the drug.[18] In certain individuals this may be an expression of a common sensitivity to all molds such as are present in fungus infections of the feet. Delayed sensitivity to penicillin occurs in 5 to 10 per cent of cases, resembles serum sickness, and is the result of repeated injections or topical applications. Manifestations include urticaria, angioneurotic edema, myalgia, and arthralgia.

The earlier preparations of streptomycin frequently gave rise to a histamine-like reaction with flushing of the skin. Acute toxic reactions with headache, palpitation, arthralgia, and delayed fever occasionally occur, especially with doses over 5 gm. per day. Studies on kidney and liver function, and on cellular blood constituents show no disturbance after streptomycin administration.

The only chronic toxic effects have been reported from Mayo Clinic[1] where patients with tuberculosis have been receiving streptomycin over many months.

In some, after three to six weeks' daily therapy, a loss of equilibrium manifests itself. This does not constitute a contraindication to therapy since loss of vestibular function will be completely compensated for eventually. In other cases, after a long period of therapy the patient has noted a low-pitched continuous tinnitus which indicates the onset of nerve deafness for low tones.[1] When this occurs the drug should be discontinued. In an otherwise normal eighth nerve, the hearing probably will return to normal if the drug is discontinued.

BACITRACIN

It seems appropriate to mention the most promising of the newer, as yet untested, antibiotic materials. This is *bacitracin* produced by a strain of Bacillus subtilis, which was cultured at the Presbyterian Hospital [12] from the compound tibial fracture of a patient named Tracy, from whom the antibiotic derives its name. The material is water-soluble, stable, and effective *in vitro*, and *in vivo* in animals, against streptococcus, staphylococcus, and clostridium. Clinical trials show it to be non-toxic. Further investigations need to be done to determine its clinical usefulness.

SUMMARY

With the application of the antibiotic substances to the treatment of infections, a very important new principle has been introduced to practical therapeutics. Newer and more powerful agents will undoubtedly be discovered. This in no way, however, lessens the need for the application of the all-important principles of good sound surgical practice.

REFERENCES

1. Brown, H. A., and Hinshaw, H. C.: Toxic reaction of streptomycin on the eighth nerve apparatus, Proc. Staff Meet. Mayo Clin., 21:347 (Sept. 4), 1946.

2. Coghill, R. D., Osterberg, A. E., and Hazel, G. R.: The relative effectiveness of pure penicillin G, X, and K, Science, 103:709 (June 14), 1946.

3. Crile, G., Jr.: Peritonitis of appendiceal origin treated with massive doses of penicillin; report of 50 cases, Surg., Gynec. and Obst., 83:150 (Aug.), 1946.

4. DeBakey, M. E., and Pulaski, E. J.: An analysis of the experience with streptomycin therapy in United States Army hospitals; Preliminary Report, Surgery, 20:749 (Dec.), 1946.

5. Dugvid, J. P.: The sensitivity of bacteria to the action of penicillin, Edinburgh M. J., 53:401 (Aug.), 1946.

6. DuVignead, V., Carpenter, F. H., Holley, R. W., Livermore, A. H., and Rachele, J. R.: Synthetic penicillin, Science, 104:431 (Nov. 8), 1946.

7. Eagle, H., and Musselman, A.: The low therapeutic activity of penicillin K relative to that of penicillins F, G, and X and its pharmacological basis, Science, 103:618 (May 17), 1946.

8. Fauley, G. B., Duggan, T. L., Stormont, R. T., and Pfeiffer, C. C.: The use of penicillin in the treatment of peritonitis; an experimental study, J.A.M.A., 126:1132 (Dec. 30), 1944.

9. Hanan, J. T.: Sublingual administration of penicillin, J. M. Soc. New Jersey, 43:127 (Apr.), 1946.

10. Heilman, D. H., Heilman, F. R., Hinshaw, H. C., Nichols, D. R., and Herrell, W. E.: Streptomycin absorption, diffusion, excretion and toxicity, Proc. Staff Meet. Mayo Clin., 20:408 (Oct. 31), 1945.

11. Humphrey, J. H., and Joules, H.: Penicillin inhalation in pulmonary disease, Lancet, 2:221 (Aug. 17), 1946.

12. Johnson, B. A., Anker, H., and Meleney, F. L.: Bacitracin; new antibiotic produced by member of bacillus subtilis group, Science, 102:376-377 (Oct. 12), 1945.

13. Keefer, C. S., (et al): Streptomycin in the treatment of surgical infections, J.A.M.A., 132:4 (Sept. 7), 1946.

14. Kozoll, D. D. (et al): The use of tyrothricin in surgical infections, Surg., Gynec. and Obst., 83:323-342 (Sept.), 1946.

15. Lyons, C.: Chemotherapy in the management of wounds, J.A.M.A., 133:215 (Jan. 25), 1947.

16. Meakins, J. C., Smith, F., and Gold, M. A.: A comparative study of some commercial preparations of oral penicillin, Canad. M.A.J., 55:97 (Aug.), 1946.

17. Meleney, F. L.: Penicillin in the treatment of established surgical infections, Ann. Surg., 124:962-980 (Nov.), 1946.

18. Morginson, W. J.: Toxic reactions accompanying penicillin therapy, J.A.M.A., 132:915 (Dec. 14), 1946.

19. Pulaski, E. J.: Streptomycin in surgical infections. Infections of the genito-urinary tract, Ann. Surg., 124:392 (Aug.), 1946.

20. Robinson, H. J., Smith, D. G., and Graessle, O. E.: Chemotherapeutic properties of streptomycin, Proc. Soc. Exper. Biol. & Med., 57:226 (Nov.), 1944.

21. Romansky, M. J.: The current status of calcium penicillin in beeswax and peanut oil; data from a study of 600 cases and clinical observation of 4000 patients given 60,000 injections, Am. J. Med., 1:395 (Oct.), 1946.

22. Rose, D., and Hurwitz, D.: The regional injection of penicillin in local infections, New England J. Med., 234:291 (Feb. 28), 1946.

23. Seager, L. D., Shoemaker, W. G., and Wells, G.: Blood levels of penicillin after various forms of oral administration, Am. J. M. Sc., 212:90 (July), 1946.

24. Seeberg, V. P., Illg, P. L., and Brown, D. J.: The gastro-intestinal absorption and destruction of penicillin, J. Am. Pharm. A. (Scient. Ed.), 35:280 (Sept.), 1946.

25. Waksman, S. A., Bugie, E., and Schatz, A.: The isolation of antibiotic substances from soil microorganisms with special reference to streptothricin and streptomycin, Proc. Staff Meet. Mayo Clin., 19:537 (Nov. 15), 1944.

26. Zintel, H. A., Wyle, M., Nichols, M., and Rhoads, J. E.: The use of streptomycin in surgical patients, Surgery, 21:175 (Feb.), 1947.

ACUTE ILEOCOLITIS

A Case Report

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A WOMAN, aged 25 years, was admitted to the hospital on June 25, 1945, with a diagnosis of acute appendicitis. She gave a history of vague abdominal pains for two weeks in the right lower quadrant. The pain was worse after meals. At 3 a.m. on the day of admission she was awakened by severe abdominal pain. This pain did not radiate to the back or lower extremities. Vomiting occurred once but diarrhea or chills did not occur. The last menstrual period was normal and urinary disturbances were absent. There was one child, aged three years.

Physical examination revealed a well developed, well nourished female who was acutely ill. She appeared more ill than one would expect from ordinary acute appendicitis. The only positive findings were marked tenderness and spasm in the right lower quadrant of the abdomen and marked tenderness and fullness in the right fornix. Movement of the cervix caused severe pain in the right side. A rectal examination revealed tenderness in the right side. The temperature was 102° F. and pulse 100. Erythrocytes numbered 5,100,000; leukocytes 25,200 (97 per cent neutrophils). The sedimentation rate was slightly increased and urinalysis was negative.

Acute salpingitis with pelvic peritonitis was suspected. The patient was placed in the Fowler position and was given 15,000 units penicillin every three hours. Three days later, since the tachycardia and fever did not subside, 1 gm. of sulfadiazine was given every three hours. Two days thereafter, on June 30, 1945, the patient seemed much better. The temperature still fluctuated between 100° and 104° F., but there was less abdominal pain. A tender and fluctuant localized mass could be felt in the right lower abdomen. An appendiceal abscess was suspected at this time. Under spinal anesthesia a small transverse incision was made in the right lower abdomen. A small amount of clear serous fluid was present. About 15 inches of ileum was found to be red, swollen and hard, with a solid feel like a tumor mass.

The cecum was similarly involved but the inflammation stopped abruptly a short distance above the ileo-cecal valve. Parts of the ileum were adherent to the right tube, ovary and uterus. The whole mass was adherent to the adjacent walls and no attempt was made to locate the appendix. The abdomen was closed. Convalescence was uncomplicated. The temperature fluctuated between 100° and 104° F., the pulse between 90-120, but the patient expressed herself as feeling better and she looked better. The leukocyte count varied between 12,400 and 29,000 and the sedimentation rate between 26 and 31 mm. in one hour.

On July 2 the sulfadiazine and on July 4 the penicillin was discontinued. Subjective improvement continued. The mass in the right side gradually disappeared so that it could not be felt; the pelvic mass and tenderness also disappeared.

On July 12 a sore throat was noted and impaired resonance was discovered at the base of the left lung. Two hundred fifty cc. of clear straw colored fluid was removed from the left pleural sac. The temperature varied between 99.4° and 102° F. Penicillin was resumed, 20,000 units administered intravenously every three hours.

On July 16 the patient's condition was unchanged; penicillin was discontinued and sulfadiazine 2.0 gm. every four hours begun. Two days later all medication was stopped. The fever gradually subsided and there was much subjective improvement. Tuberculin tests were negative. An x-ray of the chest was clear.

On July 29 the temperature rose to 103° F., leukocytes numbered 19,000 and non-radiating pain was first noted in the left middle quadrant of the abdomen.

An excretory urogram showed dilatation of the ureter and pelvis of the left kidney. Subsequently a well localized mass developed in the left middle abdominal quadrant. Muscles in this area were rigid and tender. Again an abscess was suspected. Under local anesthesia a small transverse incision was made directly over the mass. In the left colon was found a hard granulomatous mass similar in feel and appearance to that in the cecum and ileum. It was adherent to the surrounding tissues. The abdomen was closed.

Penicillin therapy was resumed and emetin HCL 0.0325 gm. (gr. ½) was administered twice daily. The fever gradually subsided to normal and there was marked improvement in the general condition.

Six days later emetin was stopped because of generalized body pains and fever and was replaced by carbarsone, 0.25 gm. twice a day. Subsequently generalized urticaria developed; temperature rose to 103° F., and there was severe headache. Penicillin was discontinued.

Two weeks postoperatively the patient felt perfectly well and the temperature and pulse were normal. Pain and tenderness in the abdomen were lacking and no masses could be felt. The incisions had healed by first intention. Leukocytes numbered 7,900.

One year later in a letter the patient said she was perfectly well and had had no recurrence of any trouble.

COMMENT

The relationship of the emetin and carbarsone to the patient's recovery is an open question. Ameba were not found on two stool examinations. One sigmoidscopic examination performed during the illness was negative for ulceration and ameba. Penicillin and sulfadiazine only partially controlled the disease.

Inflammation in the descending colon appeared one week after all medication had been stopped. The greatest improvement seemed to occur after the administration of emetin and carbarsone.

In 1932 Crohn,[4,5] Ginsburg and Oppenheimer, described a group of benign non-specific granulomas which were confined to the terminal ileum. They used the term regional ileitis to describe this pathological and clinical entity. The clinical features in these cases were diarrhea, lower abdominal pain, fever, loss of weight, and anemia. Some patients presented symptoms of partial obstruction and some cases were complicated by internal or external fistula. Since then, many terms have been used by other observers in somewhat similar cases, i. e., enteritis, chronic segmental ileitis, ileitis with segmental colitis, and ileocolitis.

It was later learned that the same pathologic and clinical features of ileitis may be found anywhere in

the ileum or jejunum and that in so called "skip" areas between the normal segment of bowel there were frequent occurrences. At first it was believed that the disease was limited to the small bowel, but cases appeared in the literature which described involvement of the cecum and other parts of the large intestine. Bockus [1,2] and his associates reported nine cases of involvement of the large bowel in a series of 21 cases of ileitis. The rectosigmoid was seldom involved.

The disease generally runs a chronic course but a few cases have appeared which suggest an acute phase. The case reported here fits in with the acute aspects of the disease as described by Gruenfeld,[9] Felsen,[7] Clute,[3] De Courcey,[6] Jackson,[10] and Smithy.[12]

Until Crohn, Ginsburg and Oppenheimer [4] clarified the clinical entity, the disease was confused with intestinal tuberculosis and malignant lesions.

PATHOLOGY

The involved ileum appears thickened, rigid, hose-like, and when palpated seems to lack a lumen. The serosa shows various degrees of hyperemia and plastic exudate. The mesentery of the involved ileum is thick and boggy and edematous. Perforations may result in fistulas or matting together of the various loops; when opened, the resected bowel reveals marked thickening of the bowel wall, marked narrowing of the intestinal lumen and mucosal ulceration, with hyperplasia. All layers of the intestine are thickened but the submucosa shows the greatest increase in breadth.

SYMPTOMATOLOGY

The symptoms depend on the stage and extent of the disease. In acute ileitis the symptoms suggest acute appendicitis or peritonitis. In the chronic cases the symptoms suggest mild ulcerative colitis with diarrhea and cramps, and in the advanced stages perforations with abscess or fistula may be present. Fever is present in the acute but is less marked in the chronic stages of the disease.

PHYSICAL EXAMINATION

Physical examination may reveal a mass in about 50 per cent of the cases. Tenderness is generally present and the x-ray findings are characteristic. Kantor,[12] introduced the term "string sign" for the marked narrowing of the lumen of the ileum. Often a defect can be demonstrated in the cecum, caused by the pressure of the thickened ileum and mesentery against the mesial portion of the cecum and colon. Smithy's cases showed no string sign in the acute phase and all his cases made complete recovery.

TREATMENT

The acute phase of ileitis should be treated medically. The treatment of the chronic stage of the disease is surgical.[9] Some physicians prefer ileo-transverse colostomy with exclusion, while others prefer resection of the diseased area. The latter carries a much higher mortality.

SUMMARY

1. A case of ileocolitis with involvement of the cecum and subsequent migration is presented.
2. Sulfonamides and penicillin seemed to control but not cure the infection.
3. Improvement followed the use of emetin and carbarsone.

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REFERENCES

1. Bockus, H. L.: Gastroenterology, Vol. No. 2, 1944.

2. Bockus, H. L., Lee, W. E.: Regional (terminal) ileitis, Ann. Surg., 102:412 (Sept.), 1935.

3. Clute, H. M.: Regional ileitis; Report of two cases, S. Clin. of N. A., 13:561 (June), 1934.

4. Crohn, B. B., Ginsburg, Oppenheimer, G. M.: Regional ileitis, J.A.M.A., 99:1323 (Oct. 15), 1932.

5. Crohn, B. B.: Regional ileitis, S. G. & O., 68:314 (Feb.), 1934.

6. De Courcey, J. L.: Terminal ileitis simulating acute appendicitis; case report, J. Med., 15:216 (June), 1934.

7. Felsen, J.: The relationship of bac. dysentery to distal ileitis, chr. ulcerative colitis and nonspecific intestinal granuloma, Ann. Int. Med., 10:645 (Nov.), 1936.

8. Garlock, J. H., Ginsberg: Regional ileitis, Ann. Surg., 116:906 (Dec.), 1942.

9. Gruenfeld, G. S., Probstein, J. G.: Acute regional ileitis, Ann. Surg., 103:273 (Feb.), 1936.

10. Jackson, W. A.: Localized hypertrophic enteritis, Brit. J. Surg., 12-27 (July), 1934.

11. Kantor, J. L.: Regional ileitis—its Roentgen diagnoses, J.A.M.A., 103:2016 (Dec. 29), 1934.

12. Smithy, H. G.: Surgery, Vol. 13, p. 122-130.

MEDICAL PROGRESS:

Recent Progress in Pulmonary Mycotic Infections*

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THIS discussion is limited to coccidioidal infection and certain aspects of pulmonary calcifications associated with sensitivity to histoplasmin. We do not infer that progress has been restricted to those subjects. It continues in actinomycosis, blastomycosis, sporotrichosis and moniliasis as well as in the superficial mycoses. Restriction of space necessitates focusing our attention.

For those in the West, coccidioidal infection poses the outstanding problem of pulmonary mycoses. It is the only one yet recognized as occurring significantly within this area, although we do see sporadic actinomycosis. The status of knowledge regarding coccidioidal infection prior to these recent developments was admirably summarized by Beck, Dickson and Rixford in 1931.[4] The one noteworthy advance between that monograph and our present era was the recovery of *Coccidioides* from soil near Delano, Kern County, by Stewart and Meyer.[74] Then, just ten years ago, the "renaissance period in the study of coccidioidomycosis" [54] was ushered in by the discovery of Gifford [36] and Dickson [23] that benign coccidioidal infection could occur in the form of coccidioidal erythema nodosum ("Valley Fever"). Subsequent reports [18,28,44,48,66,73,79] furthered our knowledge regarding this entity, gave significant evidence regarding the epidemiology of coccidioidal infection and confirmed the importance of the coccidioidin skin test. It was during this same period that the coccidioidal endemic area was proven to extend beyond the confines of the San Joaquin Valley and even of California. Also, the importance of pulmonary cavitation began to be appreciated.

The greatest stimulus to our knowledge, however, came with the introduction of vast numbers of susceptible military personnel into the arid southwest because of its ideal training conditions. The potential dangers were appreciated in the Surgeon General's Office and the Air Surgeon's Office by such men as Generals S. Bayne-Jones and Charles R. Glenn and Dr. Francis G. Blake, president of the Army Epidemiological Board. Their prompt action insured a pattern of study and control which added significantly to our knowledge and minimized infection and death. Moreover, moving into this picture was Army physician personnel with fresh viewpoints and great energy. Their contributions are continuing as they carry this knowledge into civilian life. In the over-all picture should be mentioned the splendid review of literature prepared by Forbus and Bestebreurtje [34] and the monograph prepared by Lee, Nixon and Jamison [49] which succinctly summarized the then current knowledge. At this point it seems desirable to indicate certain specific aspects of this newer knowledge.

One of the most important outgrowths of the war experience has been better recognition of the coccidioidal endemic area. The distribution of coccidioidal infection up to this period was critically reviewed in 1942 by Schenken and Palik [62] and in 1943 by Baker, Mrak and Smith.[2] Previously reported isolated cases or coccidioidin sensitizations originating in Texas,[10a,33,51,71a,b] Arizona [8,29,30,59,76,85] and California outside the endemic area [2,4,48] have been extended by civilian and military experiences. In Texas the area extends along most of the Mexican Border and includes a large part of western Texas.[64,10b,40,49,71c] It covers southern New Mexico and southern and central Arizona.[1,3,24,49,50,77] The southern tip of Nevada and southwest Utah also seem included. In California the most highly endemic area is the southern San Joaquin Valley. Further north at Merced [70] and Modesto [12] the incidence becomes very spotty. The endemic area along the west side of the Valley extends farther, approximately to Tracy. The endemic area spreads into and over the Coast Range.[19,65] Although the infection is seen in the vicinity of Paso Robles and through Santa Barbara and Ventura counties, the area does not reach the coast. The status of southern Californa is not well delimited. Certainly there are spotty endemic areas in San Diego County [53] and also in San Bernardino and Riverside counties.[39,82] These facts coupled with the knowledge that merely driving through an endemic area can result in infection mean that the infection must be kept in the differential diagnosis by most physicians in the Western States. With such a peregrinating public, physicians throughout the entire country may occasionally see such a patient.

The question of where the fungus multiplies in nature is not settled. The endemic areas are arid or semi-arid. The months of July through October when it is dry and dusty provide maximal incidence. Minimal incidence occurs during the wet season.[66,70] Actually, considerable reduction in infection can be accomplished on military installations by dust control measures.[70] These facts bespeak the infectivity of the minute arthrospores and chlamydospores of the mycelial phase of *Coccidioides immitis*.[2,25] Moreover the

* This review is based on continuing investigations of coccidioidomycosis conducted by the Commission on Acute Respiratory Diseases, Army Epidemiological Board, Office of The Surgeon General, U. S. Army, Washington, D. C., at the Department of Public Health and Preventive Medicine, Stanford University School of Medicine, San Francisco, California.

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fungus has been recovered from soil.[24a,69,74] Emmons[24a,b,c] has suggested that certain wild rodents, notably pocket mice, may become infected, die, and in their carcasses the mycelia develop from the "spherules" (sporangia) of the "parasitic" phase. As he indicates, this examination of wild rodents by the experienced who can avoid the tularemia and plague so frequently encountered in coccidioidal endemic areas could provide a means of delimiting coccidioidal endemic areas. However, many would consider that a high infection in rodents would be anticipated in view of the frequent infection in humans,* cows,† sheep[5] and dogs[31] of endemic areas. Thus the rodent reservoir theory is interesting and stimulating, but it would seem fair to consider the answer as not yet settled.

Military studies[38,39,72,77,82] permitted estimation of the frequencies of the different manifestations of coccidioidal infection. At one extreme is the person with completely asymptomatic or "inapparent" infection. Such an infection can be demonstrated only by the "conversion" or "changeover" from negative to positive coccidioidin. While dosage and other factors may influence this ratio, in the southern San Joaquin Valley approximately 60 per cent of "natural" infections fall in this category. Even under conditions optimal for diagnosis only one-quarter of the infections produce clinically diagnosed disease. Around 4 per cent of the infections in white males and 10 to 25 per cent of the infections in white females are accompanied by the erythema nodosum or multiforme of classical Dickson-Gifford "Valley Fever." The proportion of these manifestations of hypersensitivity in clinically diagnosed *disease* is approximately five times as high. Various authors[39,77] have not realized that these estimates agree closely with their own, viz., that approximately 20 per cent of the clinically diagnosed cases of coccidioidal infection have erythema nodosum or multiforme.

Disseminated, "secondary" or progressive coccidioidal infection are other names for the long-recognized coccidioidal granuloma. These Army studies have indicated that approximately 1 in 400 coccidioidal *infections*, or 1 in 100 cases of diagnosed *disease* in white adult males, disseminate. The Army experience[47,50,63,72,82] also confirms the belief[36b] that there is a racial susceptibility to progressive disease. Even under identical conditions of housing, nutrition and medical care, the frequency of dissemination in coccidioidal infections and diagnosed cases of Negroes is at least ten times that of the whites.[72]

Other complications of coccidioidal infection are pleural effusion and spontaneous pneumothorax. The former, while not usual is not rare; spontaneous pneumothorax is rare. However a really important complication of the primary infection which is sometimes confused with progressive disease is coccidioidal pulmonary cavitation.

Within the past six years we have come to recognize the frequency of coccidioidal pulmonary cavitation. Prior to Winn's[83a] article on 13 such patients, occasional cases[29,86] had been reported. The unique opportunities in the military service for following the pathogenesis of the cavities by serial x-rays have yielded clearer understanding of the evolution of these cavities. Colburn's[16] study of cavity formation in three cases has been extended greatly by Jamison's[47] study of 35. Sweigert, Turner and Gillespie[77] also have described their experience with the development of these cavities. It is to be hoped that Verne R. Mason's unpublished studies as Consultant in Medicine to the Ninth Service Command will be followed through.

The diagnosis of these cases is frequently difficult since they may be sensitive both to tuberculin and to coccidioidin and their coccidioidal serology is frequently negative. In this event, only recovery of the fungus can establish the etiology. All investigators have agreed that these patients have a high degree of immunity and very rarely disseminate. Most have no symptoms and rarely should anything be done to them. The usual indication for intervention is persistent hemoptysis. The experience of Denenholz and Cheney[22] in the beneficial effect of phrenic crush has been in line with our findings. In selected cases[58,84] pneumothorax may be used. However, the indication should be absolute and one should recognize that rarely hydro- or pyopneumothorax may ensue. Moreover, some cavities not only do not close but a few actually increase in size under pneumothorax. Successful lobectomies and lobe resections for coccidioidal cavities have been carried out at various military hospitals. While the accounts have not been published, they revise our previous opinion[67,58] that such procedures are contraindicated. However, not even chemotherapy and other adjuncts of the new techniques of intrathoracic surgery make it a casual undertaking. Most pulmonary cavities will close spontaneously and very few of those which remain open seriously impair health. Their danger of dissemination is negligible.

Various articles* have indicated currently accepted methods for diagnosis of coccidioidomycosis. The coccidioidin skin test continues to serve as the first step in diagnosis. In coccidioidal erythema nodosum a 1:1000 or 1:10,000 dilution is generally sufficient. In undisseminated active infections, 1:1000 coccidioidin[38,77,82] is usually adequate. For surveys, 1:100 is probably advisable.[68] While vesiculation is frequent with such a concentration, there is no danger of disseminating or reactivating an infection, although in relatively recent infections a bout of erythema nodosum may be precipitated.[48,68] As the antigenicity of coccidioidin is negligible, it should not be withheld for fear of sensitizing or of evoking humoral antibodies which would interfere with serological tests. Results of the coccidioidin test are necessary for adequate interpretation of serological findings. Negative skin tests may result when they are performed too early. In 1:1000 dilution the coc-

*References 36c, 44, 48, 66, 70.
†References 4, 5, 6, 20, 37, 75.

* References 13, 22, 38, 39, 65, 67, 68, 77, 82, 83.

cidioidin may be negative as long as six weeks,[77] although this would be very unusual. We[68] have found that during the first week of illness, one-sixth fail to react, while during the third week the non-reactors with undisseminated infections fall to 1 per cent. On the other hand, 70 per cent of those with disseminated infections fail to react to 1:100 coccidioidin. Jacobson,[45] who pioneered its diagnostic use in coccidioidal granuloma patients, advocated 0.3 ml. of *undiluted* coccidioidin. Unfortunately, the cross reactions become much more frequent with dilutions of 1:10. Strong coccidioidin sensitivity does occur in some patients who disseminate.[68] Very frequently the sensitivity then wanes. It may be reestablished with clinical improvement so the test has some prognostic value. There is difference of opinion as to the duration of sensitivity. Cheney and Denenholz[12] have presented evidence that the sensitivity is rapidly lost when people leave coccidioidal endemic areas. However, others[66,68] have reported dissimilar experience which would indicate that sensitivity is maintained at "readable" levels over many years and that duration of sensitivity is probably independent of exposure to the fungus. The studies of Butt and Hoffman[9] have demonstrated a correlation between sensitivity to coccidioidin and coccidioidal autopsy lesions analogous to that seen in tuberculosis. The undiluted coccidioidin seems stable almost indefinitely[68] and even diluted if kept uncontaminated, it is potent for months. However, contamination, subcutaneous instead of intracutaneous injection, faulty reading and biologicals adsorbed on syringes account for errors which may confuse the test. Moreover, while there is no cross reaction with tuberculin, there is rare cross reaction with some other agents[67] typified by histoplasmin.

When the coccidioidin test has been performed, if it is positive and there is clinical evidence of an active coccidioidal infection which is not disseminated, serological tests† may be useful. If dissemination is suspected, even a negative coccidioidin warrants these follow-up tests. In view of the persistence of coccidioidin sensitivity, a mere positive coccidioidin is no indication for serological tests. Moreover, unless dissemination is suspected, a negative coccidioidin should screen out the serological test. In patients who do not disseminate, the humoral antibodies are not present prior to development of coccidioidin sensitivity. With very mild infections, serology may never become positive. Generally, precipitins develop earlier and vanish sooner than do the complement fixing antibodies. The latter appear to have important prognostic value, for only very rarely are they negative in progressive disease.

Identification of the causative organism, *Coccidioides immitis*, provides conclusive diagnosis. Demonstration of the doubly refractile spherule or "sporangium" with endospores and without budding is possible in tissue sections. Unfortunately, unless one fulfills these criteria, errors do occur. Recently, DeLamater and Weed of Mayos[21] believed they demonstrated budding of *Coccidioides* in animal tissue. These confusing structures, noted by other investigators, are probably adherent fungus cells. They may result from incomplete separation of sporangia developed from injected mycelial fragments[2] or from incomplete cleavage or separation of adjacent endospores of sporangia.[26] However, the conservatism of the Mayo workers is certainly justified in demanding the identification of endosporulation in the sporangia. These observations also emphasize the hazards of diagnosis by coverslip examination of sputum or pus. While culturing is hazardous because of the frequency of laboratory infections when mycelia are handled, structures in sputum or even pus which are thought to be *Coccidioides* frequently are not. Besides the usual Sabouraud's or malt extract media, useful differential media[80,67] are now available. The suspected culture should be injected into mice or guinea pigs[67] to confirm the identity. Tager[78] has suggested intranasal instillation and in his hands the technique has appeared successful. Because of the theoretical risk of infection through expulsion of droplets containing the suspension, we have continued to inject the suspension intraperitoneally in our mice. The suggestion has been made by Wilhelm[80] that the suspending fluid be introduced by needle and luer through the cotton stopper if the fungus has been grown on test tube slant. Particularly in patients with pulmonary cavities wherein both tuberculin and coccidioidin tests are positive and complement is not fixed, the only hope of diagnosis is by demonstration of the etiological agent. In this event, there is no substitute for coccidioidal cultures. The point recently emphasized by Cherry[13] that active tuberculosis and coccidioidomycosis may coexist also should be borne in mind.

The elevation of the sedimentation rate with active coccidioidal infection has been mentioned frequently. It is useful in following the course of the infection. While not diagnostic, the eosinophilia which often accompanies coccidioidal disease may be a helpful lead. Willett and Oppenheim[81] recently emphasized that this eosinophilia may result in confusion of coccidioidomycosis with Loeffler's syndrome of transitory pulmonary infiltration associated with eosinophilia. One of their coccidioidal patients had a record breaking 89 per cent eosinophiles in a total white count of 49,650. In spinal fluid from patients with coccidioidal meningitis the cells are, as in tuberculous meningitis, predominantly lymphocytes. However, in the relatively few polymorphonuclear cells there is frequently a disproportionate number of eosinophiles. Even more useful in differentiation is the frequency of the "paretic" form of the colloidal gold curve. Allusion has already been made* to more recent contributions to our knowledge of the roentgenological aspects of coccidioidal infection. Others[7,15,60] also have added to the basic information in which Carter[11] pioneered. While not diagnostic, the roentgenogram is another aid in alerting the physician.

† References 13, 22, 38, 67, 77, 82, 83.

* References 16, 22, 30, 38, 47, 49, 58, 77, 82, 83.

As yet no specific drug is available for treatment. In turn the sulfonamides, penicillin and streptomycin have failed. Streptothricin [61] like tyrothricin may aid in superficial lesions. Both antibiotics are too toxic for systemic use. Coccidioidin in various forms continues to be used at times and in some instances possibly helps. However, it is very difficult to assess the efficacy of treatment in a condition where the fatality rate is 50 per cent. There is even on record one apparent recovery from coccidioidal meningitis. Every known therapeutic measure has been attempted in treating this condition but without success. This patient reported by Sweigert [77] had no treatment other than general supportive measures. It is fair to say that only in the hands of Jacobson [46] has a high level of cures by vaccine or coccidioidin been attained. The plan of restricting activities while the patient has fever and other signs of active infection, elevated sedimentation rate, rising titer of complement fixation or the roentgenological evidence of progressive pulmonary involvement remains the only suggestion. Even the beneficial effect of rest has been impugned by some skeptics. Nevertheless, even if dissemination has occurred, rest and the regime prescribed for the tuberculous continue to seem advisable.

The association of pulmonary calcifications with coccidioidal infections has been recognized for some years. Cox and Smith [17] presented experimental as well as autopsy material establishing its occurrence. These autopsy findings have been extended greatly and correlated with coccidioidin sensitivity by Butt and Hoffman.[9] The studies of Aronson and his associates [1] not only proved there was no cross reaction between tuberculin and coccidioidin and verified the geographic localization of coccidioidal infection but also gave strong evidence supporting frequency of pulmonary calcification due to coccidioidal infection. Our conception of complete specificity of coccidioidin was supported by the findings of others.[52] However, we received reports [55] of reactions in Ohio to stronger concentrations of coccidioidin. Moreover, Emmons [24b] discovered cross reaction between coccidioidin and haplosporangin, a comparable product from his Arizona fungus, *Haplosporangium parvum*. Then in our Army studies we began obtaining occasional "equivocal" and even rare positive reactions to 1:100 coccidioidin in soldiers immediately after they detrained. They denied ever having been in the West previously. These reactions occurred in personnel especially from the Ohio River area but also from most of the Mississippi Basin. Accordingly in 1943 [67] we called attention to this fact and mentioned that it corresponded to the areas of recognized histoplasmosis and of frequent pulmonary calcification in the tuberculin negative.

Christie and Peterson undertook the preparation of histoplasmin and the careful investigation of the association of sensitivity to histoplasmin and pulmonary calcification. They also sought for a syndrome of histoplasmosis comparable to primary coccidioidomycosis. Their first paper [14a] presents an excellent review of the problem of pulmonary calcifications in non-tuberculous. In a group of 181 Tennessee children, they noted pulmonary calcifications in 44 per cent. Of these 78 children with calcifications, 62 per cent were histoplasmin positive and tuberculin negative, while only 6 per cent were tuberculin positive and histoplasmin negative. They presented other data supporting this association of histoplasmin sensitivity and pulmonary calcification. Subsequent papers [14b,c] have extended their observations and among 610 Tennesseeans with pulmonary calcifications, 71 per cent were histoplasmin positive, tuberculin negative and 3 per cent tuberculin positive, histoplasmin negative. Sixteen per cent reacted to both materials. The age distribution of pulmonary calcification followed that of histoplasmin sensitivity rather than that of tuberculin sensitivity. Their sectional distribution of histoplasmin sensitivity within Tennessee paralleled the pulmonary calcifications. Their studies of geographic distribution by states also supported an association between the histoplasmin sensitivity and pulmonary calcification. However, they have been careful to indicate that as yet conclusive proof of causal relationship between pulmonary calcifications and histoplasmosis remains lacking.

The exceedingly extensive studies of the Tuberculosis Control Division of the United States Public Health Service are bringing a tremendous volume of evidence for this association. Palmer's initial investigation [57a] included 3,105 student nurses with 294 pulmonary calcifications. In the latter, only 6.8 per cent were tuberculin positive and histoplasmin negative while 67 per cent were histoplasmin positive and tuberculin negative. Only 1.2 per cent reacted neither to tuberculin nor to histoplasmin. Thus the experiences of the two groups are in substantial agreement. Palmer's subsequent paper [57b] dealing with the geographic differences in histoplasmin sensitivity in over 8,000 nurses indicated that the highest prevalence of histoplasmin sensitivity is in the central part of the United States.

Recognizing that Kansas City is an area of very high histoplasmin sensitivity, the Tuberculosis Control Division initiated very detailed studies in that area. One must read these papers to appreciate their careful, critical and cautious presentations. However, Furcolow et al [35] showed that in Missouri as in Tennessee, the percentage of reactors to histoplasmin increases with age, with pulmonary calcifications paralleling the rise. They found that among whites the percentage of reactors increased from five at age of two years to nearly 70 at 18 years. Consistently, the percentage among males was slightly greater than among females and among whites slightly higher than among Negroes. Ferebee and Furcolow [32] recently studied histoplasmin reactions in Kansas City siblings. Within the same family they found the factor appeared to be a broad one, "less localized than one limited by family environment." High [41] has reported that splenic calcifications in Kansas City also appeared to be associated with sensitivity to histoplasmin. Eighty per cent of the school children

of that city who had pulmonary calcification reacted to histoplasmin. Seventy-nine per cent of those with splenic calcifications were histoplasmin reactors. These were twice as great as the histoplasmin reactivity of the general school population.

Roentgenographic descriptions of these calcifications are contained in various recent publications.[14a, 41, 42, 87] Most noteworthy is the frequency with which *disseminated* (miliary or multiple bilateral) calcifications are associated with histoplasmin sensitivity. In the series of High, Zwerling and Furcolow[42] wherein 108 persons with disseminated calcifications were tested both with tuberculin and histoplasmin, 96 per cent reacted to histoplasmin, only 10 per cent reacted to tuberculin and none reacted only to tuberculin.

The other group of workers leading in the studies of histoplasmin sensitivity and pulmonary calcifications is at the National Institute of Health. It was the histoplasmin prepared by Emmons of this group which Palmer used in his studies. Neither the Christie-Peterson Vanderbilt team nor the Palmer-Furcolow Tuberculosis Control Division group is ready to commit itself to *Histoplasma capsulatum* as the sole, or even dominant etiological agent responsible for the histoplasmin sensitivity associated with pulmonary calcification. The group at the National Institute of Health is even more conservative. In their recent publication, Olson, Bell and Emmons[56] could not prove that there was statistically valid correlation in Loudoun County, Virginia, between pulmonary calcification and sensitivity to histoplasmin. Loudoun County has had a high incidence of proven histoplasmosis (four fatal human cases). Three Loudoun dogs and one mouse also were demonstrated to have been naturally infected with *Histoplasma*. While 83 per cent of the inhabitants tested reacted to histoplasmin, pulmonary calcification seemed to be more frequently associated with tuberculin sensitivity and history of contact with open tuberculosis. Moreover, Emmons, Olson and Eldridge[27] also have pointed out the cross sensitivity which exists between histoplasmin and blastomycin. Although coccidioidin shared in this to a degree, it was not sufficient to be very disturbing. Coccidioidin and haplosporangin are more apt to cross react. By studying the potency of the appropriate material, Howell[43] of the Kansas City group believes it is possible to ascertain dominant sensitivity. This has also been our experience. However, at the present stage there is danger of uncritical over-enthusiasm. This whole subject is developing rapidly, changing from month to month. Of paramount interest is ascertaining what infectious agent or agents are responsible for histoplasmin sensitivity. In all probability the etiology is mycotic and the infection or infections are so benign they are even more frequently inapparent than is coccidioidomycosis. Once the specific facts are known, there will probably be little point in attempting to pigeon hole or classify as long as one is sure that he is not dealing with tuberculosis. It is tuberculosis of which we must continue to beware. Although in many regions mycotic infections seem well-nigh universal, fortunately serious mycotic disease is rare.

REFERENCES

1. Aronson, J. D., Saylor, R. M., and Parr, E. I.: Relationship of coccidioidomycosis to calcified pulmonary nodules, Archives Pathology, 34:1:31-48 (July), 1942.

2. Baker, E. E., Mrak, E. M., and Smith, C. E.: The morphology, taxonomy and distribution of *Coccidioides immitis*, Rixford and Gilchrist, 1896, Farlowia, 1:2:199-244 (July), 1943.

3. Beare, W. K.: Primary pulmonary coccidioidomycosis, Air Surgeons Bulletin, 2:11:397-399 (Nov.), 1945.

4. Beck, M. D., Dickson, E. C., and Rixford, E.: Coccidioidal granuloma, California State Department of Public Health Bulletin, 57 (June), 1931.

5. Beck, M. D.: Occurrence of *Coccidioides immitis* in lesions of slaughtered animals, Proceedings Society Experimental Biology and Medicine, 26:6:534-536 (Mar.), 1929.

6. Beck, M. D., Traum, J., and Harrington, E. S.: Coccidioidal granuloma, occurrence in animals; reference to skin tests, Journal American Veterinary Medical Association, 78(N.S.31):4:492-499 (Apr.), 1931.

7. Benninghoven, C. D., and Miller, E. R.: Coccidioidal infection in bone, Radiology, 38:6:663-666 (June), 1942.

8. Brown, O. H.: Coccidioides infection in Arizona—Allergic factors in nodules?, Southwestern Medicine, 23:4:131-132 (Apr.), 1939.

9. Butt, E. M., and Hoffman, A. M.: Healed or arrested pulmonary coccidioidomycosis. Correlation of coccidioidin skin tests with autopsy findings, American Journal Pathology, 21:4:485-505 (May), 1945.

10. Caldwell, G. T.: (a) Coccidioidal granuloma, a report of three cases recognized in Texas, Texas State Journal Medicine, 28:5:327-333 (Sept.), 1932. (b) Secondary (granulomatous) coccidioidomycosis — coccidioidal granuloma, Texas State Journal Medicine, 38:6:376-382 (Oct.), 1942.

11. Carter, R. A.: (a) Coccidioidal granuloma: Roentgen diagnosis, American Journal Roentgenology and Radium Therapy, 25:6:715-738 (June), 1931. (b) Infectious granulomas of bones and joints with special reference to coccidioidal granuloma, Radiology, 23:1:1-6 (July), 1934. (c) Pulmonary mycotic infections, Radiology, 26:5:551-562 (May), 1936. (d) The roentgen diagnosis of fungous infections of the lungs with special reference to coccidioidomycosis, Radiology, 38:6:649-659 (Jan.), 1942.

12. Cheney, G., and Denenholz, E. J.: Observations on the coccidioidin skin test, Military Surgeon, 96:2:148-156 (Feb.), 1945.

13. Cherry, C. B., and Bartlett, A. G.: The diagnosis of acute Coccididioides immitis infections, Bulletin U. S. Army Medical Department, 5:2:190-193 (Feb.), 1946.

14. Christie, A., and Peterson, J. C.: (a) Pulmonary calcification in negative reactors to tuberculin, American Journal Public Health, 35:11:1131-1147 (Nov.), 1945. (b) Pulmonary calcification and sensitivity to histoplasmin, tuberculin and haplosporangin, Journal American Medical Association, 131:8:658-660 (June 22), 1946. (c) Histoplasmin sensitivity, Journal Pediatrics, 29:4:417-432 (Oct.), 1946.

15. Clark, D., and Gilmore, J. H.: A study of one hundred cases with a positive coccidioidin skin test, Annals Internal Medicine, 24:1:40-59 (Jan.), 1946.

16. Colburn, J. R.: Roentgenological types of pulmonary lesions in primary coccidioidomycosis, American Journal Roentgenology and Radium Therapy, 51:1:1-8 (Jan.), 1944.

17. Cox, A. J., and Smith, C. E.: Arrested pulmonary coccidioidal granuloma, Archives Pathology, 27:4:717-734 (Apr.), 1939.

18. Cronkite, A. E., and Lack, A. R.: Primary pulmonary coccidioidomycosis experimental infection with Coccidioides Immitis, Journal Experimental Medicine, 72:2:167-174 (Aug.), 1940.

19. Davis, B. L., Jr., Smith, R. T., and Smith, C. E.: An epidemic of coccidioidal infection (coccidoidomycosis), Journal American Medical Association, 118:14:1182-1186 (Apr. 4), 1942.

20. Davis, C. L., Stiles, G. W., McGregor, A. W.: Coccidioidal granuloma in calves, Journal American Veterinary Medical Association, 92(N.S.45):4:562-563 (Apr.), 1938.

21. DeLamater, E. D., and Weed, L. A.: Budding in the tissue phase of the life cycle of *Coccidioides immitis*: Preliminary report, Proceedings Staff Meeting Mayo Clinic, 21:26:505-509 (Dec. 24), 1946.

22. Denenholz, E. J., and Cheney, G.: Diagnosis and treatment of chronic coccidioidomycosis, Archives Internal Medicine, 74:5:311-330 (Nov.), 1944.

23. Dickson, E. C.: (a) Valley fever, Calif. & West. Medicine, 47:3:151-155 (Sept.), 1937. (b) Coccidioidomycosis, J.A.M.A., 111:15:1362-1364 (Oct. 8), 1938. (c) Primary coccidioidomycosis; The initial acute infection which results in coccidioidal granuloma, American Review Tuberculosis, 38:61:722-729 (Dec.), 1938. (d) Dickson, E. C., and Gifford, M. A.: Coccidiodes infection (coccidioidomycosis); II. The primary type of infection, Arch. Int. Med., 62:5:853-871 (Nov.), 1938.

24. Emmons, C. W.: (a) Isolation of coccidioides from soil and rodents, Public Health Reports, 57:4:109-111 (Jan. 23), 1942. (b) Emmons, C. W., and Ashburn, L. L.: The isolation of *Haplosporangium parvum* N. Sp. and *Coccidioides immitis* from wild rodents; Their relationship to coccidioidomycosis, Public Health Reports, 57:46:1715-1727 (Nov. 13), 1942. (c) Coccidioidomycosis in wild rodents; A method of determining the extent of endemic areas, Public Health Reports, 58:1:1-5 (Jan. 1), 1943.

25. Emmons, C. W.: Coccidioidomycosis, Mycologia, 34:4:452-463 (July-Aug.), 1942.

26. Emmons, C. W.: Personal communication.

27. Emmons, C. W., Olson, B. J., and Eldridge, W. W.: Studies of the role of fungi in pulmonary disease; I. Cross reaction of histoplasmin, Public Health Reports, 60:47:1383-1394 (Nov. 23), 1945.

28. Faber, H. K., Smith, C. E., and Dickson, E. C.: Acute coccidioidomycosis with erythema nodosum in children, Journal Pediatrics, 15:2:163-171 (Aug.), 1939.

29. Farness, O. J., and Mills, C. W.: A case of primary infection with coccidioides in lung with cavity formation and healing, American Review Tuberculosis, 39:2:266-273 (Feb.), 1939.

30. Farness, O. J.: Coccidioidomycosis, J.A.M.A., 116:16:1749-1752 (Apr. 19), 1941.

31. Farness, O. J.: Coccidioidal infection in a dog, Journal American Veterinary Medical Association, 97:3:263-264 (Sept.), 1940.

32. Ferebee, S. H., and Furcolow, M. L.: Histoplasmin sensitivity among Siblings, Public Health Reports, 62:23:834-847 (June 6), 1947.

33. Foley, M. P., Love, J. G., Broders, A. C., and Heilman, F. R.: Coccidioidal granuloma—Report of a case originating in Texas, Western Journal Surgery, Obstetrics and Gynecology, 48:12:738-741 (Dec.), 1940.

34. Forbus, W. D., and Bestebreurtje, A. M.: Coccidioidomycosis; A study of 95 cases of the disseminated type with special reference to the pathogenesis of the disease, Military Surgeon, 99:5:653-719 (Nov.), 1946.

35. Furcolow, M. L., High, R. H., and Allen, M. F.: Some epidemiological aspects of sensitivity to histoplasmin and tuberculin, Public Health Reports, 61:31:1132-1144 (Aug. 2), 1946.

36. Gifford, M. A.: (a) Annual report Kern County Health Department for the fiscal year July 1, 1935, to June 30, 1936, pp. 22-23. (b) Gifford, M. A., Buss, W. C., and Douds, R. J.: Annual report Kern County Health Department for the fiscal year July 1, 1936, to June 30, 1937, pp. 39-54. (c) Coccidioidomycosis in Kern County, California, Proceedings Sixth Pacific Science Congress of the Pacific Science Association, 5: pp. 791-796, University of California Press, Berkeley, Calif., 1942.

37. Giltner, L. T.: Occurrence of coccidioidal granuloma (oidioidomycosis) in cattle, Journal Agricultural Research, 14:533-541 (Sept. 16), 1918.

38. Goldstein, D. M., and Louie, S.: Primary pulmonary coccidioidomycosis, Report on an epidemic of 75 cases, War Medicine, 4:9:299-317 (Sept), 1943.

39. Goldstein, D. M., and McDonald, J. B.: Primary pulmonary coccidioidomycosis (follow-up of 75 cases with 10 more cases from a new endemic area), J.A.M.A., 124:9:557-571 (Feb. 26), 1944.

40. Haynes, D. M., and Hess, W. I.: Cutaneous test with coccidioidin; review of the literature and a report of a series in Texas, Journal Laboratory and Clinical Medicine, 31:12:1317-1324 (Dec.), 1946.

41. High, R. H.: Calcifications in the spleen; occurrence in histoplasmin and tuberculin reactors, Public Health Reports, 61:49:1782-1786 (Dec. 6), 1946.

42. High, R. H., Zwerling, H. B., and Furcolow, M. L.: Disseminated pulmonary calcification: A report of one hundred and thirteen cases, Public Health Reports, 62:1:20-29 (Jan. 3), 1947.

43. Howell, A.: Studies of fungus antigens: I. Quantitative studies of cross-reactions between histoplasmin and blastomycin in guinea pigs, Public Health Reports, 62:18:631-651 (May 2), 1947.

44. Hurwitz, S., Young, J. E., and Eddie, B. V.: Coccidioides immitis intradermal skin reaction; Preliminary report of 449 cases, Calif. & West. Medicine, 48:2:87-89 (Feb.), 1938.

45. Jacobson, H. P.: (a) Coccidioidal granuloma: Specific allergic cutaneous reaction; experimental and clinical investigations, Archives Dermatology and Syphilology, 18:4:562-567 (Oct.), 1928. (b) Fungus diseases, p. 235, p. 246, Charles C. Thomas, Baltimore, Md., 1932.

46. Jacobson, H. P.: Immunotherapy for coccidioidal granuloma; Report of cases, Archives Dermatology Syphilology, 40:4:521-540 (Oct)., 1939.

47. Jamison, H. W.: A roentgen study of chronic pulmonary coccidioidomycosis, American Journal Roentgenology and Radium Therapy, 55:4:396-412 (Apr.), 1946.

48. Kessel, J. F.: (a) The coccidioidin skin test, American Journal Tropical Medicine, 19:2:199-204 (March), 1939. (b) Recent observations on coccidioides infection, American Journal Tropical Medicine, 21:3:447-453 (May), 1941.

49. Lee, R. V., Nixon, N., and Jamison, H. W.: Syllabus on coccidioidomycosis, Coccidioidomycosis Control Program for the A.A.F.W.F.T.C., Prepared by Headquarters Army Air Forces Western Flying Training Command, Office of the Surgeon, Santa Ana, California, (various editions 1942-1944).

50. Lee, R. V.: Coccidioidomycosis in the Western Flying Training Command, Calif. & West. Medicine, 61:3:133-134 (Sept.), 1944.

51. Lehman, C. F., and Pipkin, J. L.: Coccidioidal granuloma (chronic hypertrophic), Archives Dermatology and Syphilology, 31:4:586-589 (Apr.), 1935.

52. Lewis, G. K., and Hopper, M. E.: An introduction to medical mycology, p. 194, Year Book Publishers, Chicago, Ill., 1943.

53. McKenney, F. D., Traum, J., and Bonestell, A. E.: Acute coccidioidomycosis in a mountain gorilla (Gorilla Beringeri) with anatomical notes, Journal American Veterinary Medical Association, 104:3:136-140 (Mar.), 1944.

54. Meyer, K. F.: Discussion of paper by Dickson, E. C.: Valley fever, Calif. & West. Medicine, 47:3:155 (Sept.), 1937.

55. Nelson, W. E., and Furcolow, M. L.: Personal communications.

56. Olson, B. J., Bell, J. A., and Emmons, C. W.: Studies on histoplasmosis in a rural community, American Journal Public Health, 37:4:441-449 (Apr.), 1947.

57. Palmer, C. E.: (a) Nontuberculous pulmonary calcification and sensitivity to histoplasmin, Public Health Reports, 60:19:513-520 (May 11), 1945. (b) Geographic differences in sensitivity to histoplasmin among student nurses, Public Health Reports, 61:14:475-487 (Apr. 5), 1946.

58. Peers, R. A., Holman, E. F., and Smith, C. E.: Pulmonary coccidioidal disease, American Review Tuberculosis, 45:6:723-740 (June), 1942.

59. Phillips, E. W.: Presence of coccidioidal infection in Phoenix, Southwestern Medicine, 23:2:48-51 (Feb.), 1939.

60. Powers, R. A., and Starks, D. J.: Acute (primary) coccidioidomycosis: Roentgen findings in a group "epidemic," Radiology, 37:4:448-453 (Oct.), 1941.

61. Roessler, W. G., Herbst, E. J., McCullough, W. G., Mills, R. C., and Brewer, C. R.: Studies with *Coccidioides*

immitis. II. In Vitro effects of streptothricin and streptomycin, Journal Infectious Diseases, 79:1:23-26 (July-Aug.), 1946.

62. Schenken, J. R., and Palik, E. E.: Coccidioidomycosis in States other than California, with report of a case in Louisiana, Archives Pathology, 34:3:484-494 (Sept.), 1942.

63. Schlumberger, H. C.: A fatal case of cerebral coccidioidomycosis with cultural study, American Journal Medical Sciences, 209:4:483-495 (Apr.), 1945.

64. Schulze, V. E.: Acute coccidioidomycosis in West Texas, Texas State Journal Medicine, 38:6:372-376 (Oct.), 1942.

65. Shelton, R. M.: Survey of coccidioidomycosis at Camp Roberts, California, Journal American Medical Association, 118:14:1186-1190 (Apr. 4), 1942.

66. Smith, C. E.: The epidemiology of acute coccidioidomycosis with erythema nodosum ("San Joaquin" or "Valley Fever"). American Journal Public Health, 30:6:600-611 (June), 1940.

67. Smith, C. E.: Coccidioidomycosis, Medical Clinics North America, 27:3:790-807 (May), 1943.

68. Smith, C. E., Whiting, E. G., Baker, E. E., Rosenberger, H. G., Beard, R. R., and Saito, M. T.: The use of coccidioidin, Paper delivered June 19, 1947, at Annual Meeting of National Tuberculosis Association. In press.

69. Smith, C. E., and Baker, E. E.: Summary of present status of coccidioidal infection, Weekly Bulletin California State Department of Public Health, 20:29 and 30:113-115 and 117-119 (Aug. 9 and 16), 1941.

70. Smith, C. E., Beard, R. R., Rosenberger, H. G., and Whiting, E. G.: Effect of season and dust control on coccidioidomycosis, Journal American Medical Association, 132:14:833-838 (Dec. 7), 1946.

71. Smith, L. M.: (a) Coccidioidal granuloma; Report of a case originating in West Texas, Archives Dermatology and Syphilology, 28:2:175-181 (Aug.), 1933. (b) Smith, L. M., and Waite, W. W.: Coccidioidal granuloma; Report of a fatal case, Southwestern Medicine, 18:9:305 (Sept.), 1934. (c) Coccidioidal granuloma in Texas; A report of five cases with dermatological manifestations, Texas State Journal Medicine, 38:6:383-385 (Oct.), 1942.

72. Smith, C. E., Beard, R. R., Whiting, E. G., and Rosenberger, H. G.: Varieties of coccidioidal infection in relation to the epidemiology and control of the diseases, American Journal Public Health, 36:12:1394-1402 (Dec.), 1946.

73. Stewart, R. A., and Kimura, Frances: Studies in the skin test for coccidioidal infection. I. Preparation and standardization of coccidioidin, Journal Infectious Diseases, 66:3:212-217 (May-June), 1940.

74. Stewart, R. A., and Meyer, K. F.: Isolation of coccidioides immitis (Stiles) from the soil, Proceedings Society for Experimental Biology and Medicine, 29:8:937-938 (May), 1932.

75. Stiles, G. W., and Davis, C. L.: Coccidioidal granuloma (coccidioidomycosis) its incidence in man and animals and its diagnosis in animals, Journal American Medical Association, 119:10:765-769 (July 4), 1942.

76. Storts, B. P.: Coccidioidal granuloma simulating brain tumor in a child of four years, Journal American Medical Association, 112:14:1334-1335 (Apr. 8), 1939.

77. Sweigert, C. F., Turner, J. W., and Gillespie, J. B.: Clinical and roentgenological aspects of coccidioidomycosis, American Journal Medical Sciences, 212:6:652-673 (Dec.), 1946.

78. Tager, M., and Liebow, A. A.: Intranasal and intraperitoneal infection of the mouse with *Coccidioides immitis*. Yale Journal Biology Medicine, 15:1:41-64 (Oct.), 1942.

79. Thorner, J. E.: Erythema nodosum in childhood associated with infection by oidium coccidioides; Report of seven cases, Archives Pediatrics, 56:10:628-638 (Oct.), 1939.

80. Wilhelm, S.: Isolation of coccidioides immitis from sputum, Bulletin U. S. Army Medical Department, 5:4:468-473 (Apr.), 1946.

81. Willett, F. M., and Oppenheim, E.: Pulmonary infiltrations with associated eosinophilia, American Journal Medical Sciences, 212:5:606-612 (Nov.), 1946.

82. Willett, F. M., Weiss, A.: Coccidioidomycosis in Southern California; Report of a new endemic area with a review of 100 cases, Annals Internal Medicine, 23:3:349-375 (Sept.), 1945.

83. Winn, W. A.: (a) Coccidioidomycosis associated with pulmonary cavitation, Archives Internal Medicine, 68:6:1179-1214 (Dec.), 1941. (b) Winn, W. A., and Johnson, G. H.: Primary coccidioidomycosis; A roentgenographic study of 40 cases, Annals Internal Medicine, 17:5:407-422 (Sept.), 1942.

84. Winn, W. A.: The treatment of pulmonary cavitation due to coccidioidal infection, Calif. & West. Medicine, 57:1:45-46 (July), 1942.

85. Woolley, M. T.: Mycological findings in sputum, Journal Laboratory Clinical Medicine, 23:6:553-565 (Mar.), 1938.

86. Yegian, D., and Kegel, R.: Coccidioides immitis infection of the lung; Report of a case resembling chronic pulmonary tuberculosis, American Review Tuberculosis, 41:393-397 (Mar.), 1940.

87. Zwerling, H. B., and Palmer, C. E.: Pulmonary calcification in relation to sensitivity to histoplasmin, Journal American Medical Association, 134:8:191-192 (June 21), 1947.

California Cancer Commission Studies*
Chapter V

Diagnosis and Radiation Therapy of Cancer

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CANCER is such a desperate disease and its diagnosis and treatment fraught with such difficulties that it might be wise to consider *consultation normal procedure* in its management.

The consultation has first to decide if it be cancer, and determine its location, extent and type. The diagnostic radiologist will often have something to offer.

Next, the consultation has to settle on a method of treatment. The radiologist has a different function here, for he is speaking as a therapist. In fact it may not even be the same person, for not all radiologists practice both diagnostic and therapeutic radiology. If definitive treatment of the cancer is deemed possible, it will be surgical or radiological, or both, (medicinal treatment of cancer is as yet hardly developed—nitrogen mustards and radio-phosphorus are about all the drugs we have so far). The surgeon or the radiologist may take over as a practitioner of the medical art according to his specialty, or they may team up where radiation must be applied by surgical approach, and may come together again in face of threatened or actual recurrence.

Now these consultations may be formal ones, but many a one is quite informal. The medical profession has such a difficult job to do that every physician should stand ready to lend a helping hand to his colleague. Many consultations are given without fee, and gladly. It is not hard to tell when a physician is asking help for his patient's sake, and none of us need be self-conscious about the insufficiency of his own knowledge. This is not saying that it is other than dishonest to "mooch" an opinion from a fellow practitioner, that in all reason the patient should expect to pay for. And if the consultation is in fact paid for, then it should be the patient who pays it and not his physician.

This brings us to the most important point about consultations concerning cancer. *The first consultation should be had before treatment of any kind is decided upon.* It is very destructive to morale to abandon a method of treatment once it has been started. It is most distressing for a surgeon to be called to see a patient already under irradiation therapy, or for a radiologist to be called to advise and devise irradiation for a patient who has just been operated upon. The initiation of one kind of treatment rules out some range of other treatment, renders ineligible some modes of combinations which could have been done if engaged in from the start. And who can now tell if some one of these might not have been favorably considered? They can now hardly be mentioned—for who shall tell the patient that the course pursued was not in fact the wisest? In cancer, of all diseases, the patient's morale most needs continuous and thoughtful support.

DIAGNOSTIC RADIOLOGY

There is one roentgen examination peculiarly pertinent to cancer patients and cancer suspects, namely: The Standard Survey. This is a search for metastases in lungs and bones, where alone the x-ray is efficient in discovering them. The survey has in fact not been standarized. For some cancers, as skin, respiratory apparatus, gastrointestinal tract, testicles and uterus, metastasis to bone is uncommon and stereo chest films (together with local films of the tumor site) are a fair "survey." For others, such as breast, thyroid and kidney, the bones are a likely site. Most radiologists would consider sufficient for a "standard" survey: Stereo chest, stereo pelvis, stereo skull (lateral), lateral thoracic and lumbar spine. The pelvis films can well include the top 20 cm. of the femora.

Metastatic habits of various types and locations of cancer are noted in the sections concerned. Some general and particular radiological facts and convictions are worth bringing together in this chapter.

BONE TUMORS

Bone tumors are definitely in the realm of roentgen diagnosis. However, roentgen evidence standing alone is not to be trusted, either as to neoplasm *vs.* inflammation, nor as to malignant *vs.* benign, nor as to operable *vs.* irradiable.

Exposures of two different densities are often helpful in bone tumors.

Laminagrams will sometimes reveal an abscess cavity, differentiating sclerotic osteomyelitis from osteogenic sarcoma.

(Therapeutic test of penicillin, bismuth and maybe iodide will sometimes prove a bone tumor to be gumma. This has been known to occur even with a negative Wassermann).

CHEST

A *lateral view* should be routine when thinking of pulmonary cancer. It would be false economy to give up the lateral to get a stereo. Rather, choose to accept a plain anterior and use the second film

* Organized by the Editorial Committee of the California Cancer Commission.

for a lateral. (In survey for metastasis, just stereo anterior is the usual choice).

Fluoroscopy is needed in cases of tumors in the chest to determine:

1. Pulsation
2. Separation from hilar structures
3. Involvement or displacement of esophagus
4. Phrenic paralysis
5. To detect fluid. This is often hard to be sure of in small quantity. It can be confirmed by a posterior film taken with horizontal ray, the patient lying on the suspected side, supported on a pad so that the axillary ribs show on the film. A wafer grid and a heavy exposure are essential.

Iodized oil may demonstrate an intrusion into a bronchus, or an obstruction.

Demonstration of bronchiectatic cavities may show the cause for a shrunken lobe that would otherwise be blamed on a blocked bronchus.

The oil cannot be expected to run into abscess cavities.

Kymograms are made to demonstrate pulsation. Tumors can, however, transmit pulsation and aneurysms can be blocked with clot, preventing pulsation. Expansile pulsation can perhaps be differentiated from transmitted pulsation by *kymography*, especially if done in two directions (vertical and horizontal travel).

Laminagrams are sometimes of value in locating and identifying a pulmonary or a bronchial tumor.

BRAIN

Displacement of a calcified pineal reveals a "space filling lesion" which can be hemorrhage or cyst as well as tumor. It can also be produced by shrinkage of a lobe; in fact the first "pineal shift" in the literature was due to cerebral shrinkage after apoplexy. To demonstrate lateral "shift" one needs posterior or anterior projections absolutely true, without any obliquity. It is probably better to judge the midline from nasal septum and lambda and odontoid (especially as seen in stereo) than to measure from pineal to temples or parietes. In lateral view one refers to Vastine's statistics for the range of normal position. (Figure 1.)

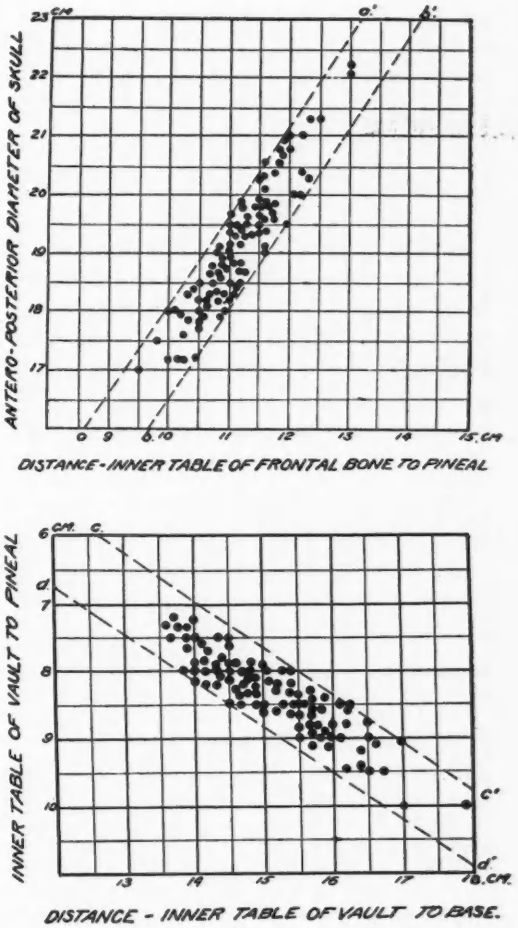

Figure 1.—Vastine's data for range of position of the (calcified) pineal as seen in lateral skull films of normal subjects.

Laminagraphy can reveal a calcified pineal, otherwise lost in the density of midline shadows. It is best done in this case with a small angle of swing.

Air (or gas) encephalography and *ventriculography* is often essential to localize a brain tumor. However, there are cases where clinical evidence is almost incontrovertible, rendering air unnecessary.

Even with the extra operation (trephine), ventriculography is probably safer than encephalography (spinal air injection), because any subsequent dangerous increase in pressure can be promptly relieved by a trochar through the hole already made.

STOMACH

Roentgen differentiation of cancer from benign lesions is often uncertain. Ulcers close to the pylorus are reputedly more likely to be cancerous, and so are large ones anywhere, but more than this is needed for diagnosis. The rare ulcer that lies precisely on the greater curvature is cancer. Ulcers of the stomach should heal in a few weeks on good medical management. If they do not, they should be explored, lest they be in fact cancer.

Cancers of the stomach are apparently not coming to operation at an earlier stage now than they did 20 years ago. Nevertheless we should keep on trying. Gastrointestinal examinations on apparently well persons have turned up as many as one case of cancer in 500 and as few as one in 2,500.

Large size of tumor as shown in x-ray should not discourage one from operating, for operability is determined not by size but by extent of spread (metastasis). A bulky tumor is more apt to produce symptoms and come to diagnosis before metastasizing than a slow-growing, ulcerated one.

SMALL INTESTINE

The ileum and jejunum and lower portions of the duodenum have very few cancers, and those few are hard to diagnose. Films every 30 to 60 minutes after barium meal are a help. The so-called *small intestine enema*, given through a tube passed (with patience) through the pylorus into the duodenum, can sometimes demonstrate the entire length of small intestine in a few minutes. Intussusception in an adult should lead to suspicion of tumor.

COLON

Air (or oxygen) contrast added to the standard barium enema should be routine in case of suspected tumor, or where there has been bleeding by bowel. Air will often drive barium through a constriction. It will often show a polyp that is missed in first examination because completely surrounded by the barium. Air embolism is so extremely rare from inflation of the colon that we do not account the procedure dangerous. (Air is more dangerous in the bladder). Preliminary catharsis is essential, lest a scybala be mistaken for a polyp.

It is good practice to use oxygen instead of air, for it is more rapidly absorbed, shortening the patient's period of discomfort.

The films can well include two made with x-ray directed horizontally, with patient lying first on left side, then on right side.

URINARY TRACT

Excretory urography should be done in all cases of urinary bleeding. This is often a late symptom of cancer, however, and we wish we had an earlier clue, for kidney tumors often remain silent for a long time. Excretory urograms have some advantages over retrograde pyelograms, notably absence of pressure distortion and of pyelovenous and pyelolymphatic back flow, and good demonstration of muscular activity of pelves and ureters. But all the drugs used have some danger. One that is very much used (diodrast), because accepted most smoothly, has produced several deaths (in some millions of injections).

Not infrequently a suspicion turned up in excretory urograms requires confirmation by *retrograde pyelography*.

Renal cysts and tumors produce similar deformities. Polycystic kidneys are usually bilateral but not always.

The responsibility in renal diagnosis is often heavy, for the surgeon may have to remove the kidney on little more than roentgen evidence, knowing that he may still not be sure of the diagnosis after he has actually exposed the kidney to inspection and palpation. It has been said: "No exploratory operation for renal cancer," meaning that if one suspects cancer strongly enough to expose the kidney, he must go ahead and take the kidney out, realizing full well that this policy will result in removal of a few kidneys that prove after all to hold no tumor.

PNEUMOPERITONEUM

Pneumoperitoneum is seldom done. The risks of peritoneoscopy or of diagnostic laparotomy are so small that one would usually choose these instead, if diagnosis be not otherwise attainable.

THOROTRAST

Intravenous injection of thorium dioxide to discover tumor in liver (metastases usually), is under suspicion because the quantity of thorium used, measured in terms of radioactivity (a few microcuries) is similar to the known serious dose of radium in bones. Also some animal experiments have shown its capacity to induce sarcoma. However, a number of patients have carried thorotrast in the liver (and spleen) for five years or more without disaster. Its use is probably warranted whenever the diagnostic evidence it will give is important for the management of the case.

SERENDIPITY

It is a discouraging feature of cancer that it is so often painless in its early stages. Many patients carry their cancers for a long time before symptoms develop that are sufficient to call any attention to the tumor. Although few cancers are in such location as to be diagnosed by x-ray, occasionally a cancer will reveal itself in a roentgen examination done for quite other reasons. It may lie unobtrusively "at the corner of the film," but if the radiologist overlooks it, the patient loses a chance to have his cancer treated at a time when it is symptomless, therefore early, and therefore promising for cure. Radiology should always be practiced with at least half an eye to picking up such things.

RADIATION THERAPY

Irradiation has a broad though limited usefulness in the treatment of cancer. The results run from curative through temporary arrests and palliation down to frank failure. Nevertheless, the average experience, or what we call the "chances" for a particular patient, can be very much bettered by a good understanding of the physical and biological foundations, a wise clinical judgment and a skillful application. These, then, are the qualifications that must be demanded of the radiologist to whom a patient is referred for therapy. The more the referring physician knows about these things, the better for his consultations with the radiologist on the individual patient.

Radiation is destructive to living tissue. The nucleus is much more sensitive than the cytoplasm, especially when in mitosis. The range of radiosensitivity is enormous. Bacteria require many thousands of roentgens to kill them, some insects' eggs only a few hundred.

Radio-sensitivity of normal human-tissues extends from the supersensitive lymphocytes, (about ten times as sensitive as skin epithelium), to the very resistant completely differentiated muscle and nerve cells, (about ten times as radio-resistant as skin epithel-

ium). The endothelium of blood vessels is in the middle of the range and what one usually observes after irradiation of muscle or brain is actually due to the roentgen injury to the blood supply.

RADIO-SENSITIVITY OF NEOPLASMS

In general a neoplasm is more radio-sensitive than its tissue of origin, while still remaining of the same order of sensitivity. A malignant neoplasm is likely to be more radio-sensitive than its benign homologue, and the more anaplastic the tumor is, the more radio-sensitive it is likely to be.

Radio-curability is not the same thing as radio-sensitivity, and the great malignancy and spreading habit of anaplastic cancers usually more than offsets their comparative radio-sensitivity. The range among neoplasms is large. Leukemia might be affected by 10 r. A chondroma would remain uninfluenced by any ordinary clinical dose.

DOSAGE

The dose and the anatomical and temporal details of its application are the essence of the art of radiation therapy. It may seem wise to give a large dose to a radio-sensitive tumor to lessen chance of recurrence. One cannot, however, better the chances in a more radio-resistant tumor by going to enormous doses, even though the patient survive the severe reaction. Except for very small tumors there seems to be a best dose, beyond which the chance of recurrent cancer increases again.

The roentgen (r) is the unit of x-ray exposure (dose). It is measured by the ions it produces in air, 2,100,000,000 pairs per cc. Flesh being 800 times as dense, 1 r produces some 1,600,000,000,000 pairs of ions per cc. in tissue. This amounts to about 83 ergs of energy per cc. Dependable instruments are available to measure x-ray dose. The radiologist may do his own measurements or have a physicist come at intervals to calibrate his machines.

Tissue dose at the skin is usually augmented by x-rays scattered back from the mass of flesh irradiated. In a deep-seated tumor it is less than at the surface, because of absorption. This "depth dose" may be built up by irradiating a larger field and so scattering some x-ray into the tumor from the sides. More importantly it can be increased by "cross fire," i.e. irradiation from different sides (usually opposite sides). But by the latter strategem it can still not be built up centrally to as high a dose as at the surface.

Summation of dosage produced by several irradiations can be done only in terms of tissue doses produced at a certain place. It is misleading to add together the doses applied at several different skin surfaces. Radium dosage affecting the same volume of tissue can be added in by calculating the roentgen equivalent from the datum: 1 mg. with 0.5 mm. platinum filter gives 8.4 r per hour at 1 cm. distance.

Range of doses used in cancer therapy is not large, if one except the leukemias and lymphoblastomata. One would like to give carcinoma about 5000 r of tissue dose, spread over a few weeks' time. Some

TABLE 1.—*Order of Radio-sensitivity of Tumors*

Radio-sensitive

1. Leukemia (if it be a tumor. But, unfortunately, not radio curable.)
2. Lymphoblastomata
   a. Lymphosarcoma (considerable variation).
   b. Hodgkin's disease (great variation).
   c. Reticulum cell sarcoma.
3. Medulloblastoma.
4. "Lymphoepithelioma" (anaplastic carcinoma with lymphoid stroma).
   Ewing's tumor of bone (endothelial myeloma).
   Embryonal carcinoma.
   a. Testis (some variation).
   b. Ovary (much variation).
5. Giant cell tumor of bone (if it be a neoplasm).
   Wilm's tumor of kidney.
   Plasma-cell myeloma (multiple myeloma of bone. Its clinical response is worsened by its wide distribution).
   Hemangioma and hemangio-endothelioma.
   Lymphangio-endothelioma.
   Keloid and hypertrophic scars.

Moderately radio-sensitive

6. Epithelioma.
   a. Anaplastic (transitional cell).
   b. Epidermoid (when in mouth, tonsil, pharynx, larynx and especially bronchus and esophagus, the location worsens the clinical response very much).
   c. Basal cell (usual small size and lack of metastasis make the clinical response better).
7. Carcinoma of breast (moderate variation).
   Carcinoma of uterus.
   a. Epidermoid of cervix.
   b. Adenocarcinoma of cervix or fundus.
8. Carcinoma of thyroid (great variation).
   Carcinoma of ovary (great variation. Some pseudomucinous tumors may be radio-sensitive, about degree 4).
   Carcinoma of rectum (great variation. Mucoid type may be sensitive).
   Other adenocarcinoma (great variation).
9. Pinealoma.
   Retinoblastoma.
   Glioblastoma multiforme.
   Pituitary adenoma (non malignant).
10. Malignant melanoma, pigmented or non-pigmented.
    Rhabdomyosarcoma.
    A few anaplastic sarcomata of fibroblastic and neural origin.

Of doubtful radio-sensitivity

11. Fibrosarcoma.
    Hypernephroma.
    Myxosarcoma.
    Liposarcoma.
    Myosarcoma.
    Astroblastoma.

Radio-resistant

12. Glioma, with exceptions listed above.
    Meningioma.
    Craniopharyngeoma.
    Mixed tumor of parotid.
    Osteogenic sarcoma of bone (osteogenic or osteolytic).
    Leiomyoma (the fibromyoma of uterus usually regresses after menopause, natural or induced).
    Teratoma.
    Neurofibroma and ganglioneuroma, including acoustic neuroma.
    Ependymoma.
    Chondroma.
    Lipoma.
    Myxoma.
    Chordoma.
    Osteoma.

may be cured with two-thirds of that. Increase in dosage *far* above this level will not bring in the more radio-resistant ones and may spoil the success of some that would have done well at the 5000 r level. For very small lesions it is satisfactory to give the dose in a single sitting, in which case one uses only about 3000 r.

RECOVERY RATE

For doses to produce an erythema, the skin recovers 63 per cent in the first 24 hours. But with repeated treatments after that the recovery gets slower and slower, until after a month of small daily doses it amounts to about 6 per cent a day. At the level producing severe skin damage, the recovery is much slower. Recovery of the bone marrow (hematopoietic) from repeated small doses is even slower. Radiation injury to the gonads (producing genetic mutations) has been shown in animals not to be recovered from at all.

PROTRACTION AND FRACTIONATION OF DOSE

The recovery rate for the cutis (blood vessels etc.) is faster than for the epidermis. One can therefore kill the epidermis (and epidermoid cancer) with less concomitant dermal necrosis by giving the dose in daily small pieces. Such fractionation may spread the treatment over one to four weeks or longer. Some therapists have treated twice a day, some only twice a week. Some think each dose should be given slowly —3 to 5 r per min., but most find 20 to 100 r per min. satisfactory. "Contact therapy" at 10,000 r per minute works well on small lesions.

Nausea and vomiting follow large doses to large areas. Susceptibility varies and divided doses minimize. Hodgkin's disease seems to sensitize. Phenobarbital, 100 mg. given one hour before treatment, helps. Chloral can be used in case of barbiturate sensitization. Pyridoxin (Vitamin B_6) 25 mg. four times a day is good. Benadryl 50 mg. four times a day has worked in more stubborn cases. After a day or two the dose can be reduced. By-effects (lightheadedness, etc.) can be bothersome. Fluid and carbohydrate intake should be kept high.

Granulopenia often develops when very large areas are treated heavily. A count of 2,000 granulocytes seems dangerous. Penicillin may seem advisable to forestall infection.

Anemia in severe degree occurs less often and usually later. It may be hard to tell whether the x-ray or the cancer has caused it.

LOCAL RADIATION INJURIES

Erythema follows irradiation of a few hundred roentgens, with latent period one to twenty days.

Epilation requires somewhat less than an erythema dose. The hair will grow in again except after injuriously large doses. Cosmetic epilation is not to be done.

Edema often appears during a heavy course of irradiation, especially in the throat. In Hodgkin's disease it may be seen within 24 hours after as little as 100 r. It seems to lessen the chances of cure.

Epidermitis, epithelitis and mucositis are the terms applied to severe benign roentgen inflammation with desquamation of the epithelium. This is what is aimed at in the definitive treatment of localized cancer of the skin or mucous membrane.

Palliation of the local reaction may require only vaseline, but often a local analgesic is needed. Nupercainal has a high incidence of sensitization—even after a negative patch test.

RADIATION ULCERS

Indolent, indurated, painful, persistent ulceration can develop after heavy irradiation, early or after several years. Sunburn or mechanical injury can be the proximate cause. Fundamentally the ulcer is due to ischemia consequent on the roentgen destruction of vascular endothelium. Second and third heavy courses of x-ray are especially dangerous.

Treatment is often ineffective. Urea crystals can dissolve the dead collagen that clutters the base of the ulcer and sometimes lead to healing. Chlorophyll ointment is very beneficial. Radon ointment seems promising. Excision will often require a pedicle graft. Split skin grafts usually fail because of ischemic base.

Cancer often develops in x-ray and radium ulcers and scars. It must be excised. It can develop years after many small doses, even without an erythema, as some of the pioneer radiologists have personally experienced.

QUALITY OF X-RAY

Quality is a matter of wave length. Soft x-rays are of long wave length, low penetrating power, and produced by low voltage. Hard x-rays are of short wave length, great penetrating power, and produced by high voltage. A therapist should have available qualities of half value layer 1 mm. (produced at about 100 kv) up to h.v.l. 1 or 2 mm. Cu (produced at about 200 kv). Supervoltage gives only a little further increase in penetration. Superiority of biologic effect has not been proved for shorter wave lengths.

RADIUM

Radium gives alpha, beta and gamma rays.

Alpha rays are used now only in radon ointment.

Beta rays make the unfiltered radium plaque an elegant tool for the treatment of small superficial skin lesions.

Gamma rays are like very hard x-rays. The radium cannon has yielded to high voltage x-ray for external application. But there remains the field of intracavitary and interstitial irradiation where radium is irreplaceable.

Radon can substitute for its parent radium. For interstitial irradiation radon gold seeds have the advantage over radium needles in that they can be left in place. The radon decays one-half in 3.85 days and is almost gone in a month, having delivered a total equivalent to 133 mg. hr. for the usual 1 millicurie seed.

MODERN DEVELOPMENTS

The *betatron* and the *synchrotron* are machines to produce beta rays of many megavolts' energy. The beta rays can be used directly, their high energy making them penetrating enough to get into the middle of the body. Or they can be directed against a tungsten target to produce super-hard x-rays. Biological experiments have been done in some number with betatron, but the clinical usefulness in cancer therapy has not yet been much explored.

Neutron rays can be produced with a large cyclotron in amounts sufficient for clinical use. They differ from x-rays in being absorbed in tissue through production of high speed protons, instead of high speed electrons. The result is a hundred-fold increase in the specific ionization (columnar density of ionization) along the ionized tracks through the cells. One of the results is that the same number of ions is some five times as effective by neutron rays as by x-rays. But it is unproven that they cure cancer better. Certainly modern therapy tubes are infinitely more flexible mechanically than a cyclotron, making precise application cross-fire clinically attainable by x-ray, and practically beyond reach for neutron rays.

Radioactive isotopes from the cyclotron on the chain-reacting pile hold almost an infinitude of medical promise. Their widest field will be for research in physiology and biochemistry by the "tracer" technic.

Phosphorus 32 has proved useful in leukemia. Whether it will replace x-ray, or to what extent, has yet to be decided. It *seems* by far the best therapy for polycythemia vera.

Iodine 130 and 131 are capable of destroying the thyroid in situ. The clinical art of using them to control Grave's disease is still in the stage of research development.

Only the rarest thyroid carcinoma (metastasizing adenoma) will pick up iodine and so be susceptible to radio-iodine therapy.

The physical and chemical and biological and medical technics in the isotope field are so complicated and difficult that their description seems quite out of place here.

At present it seems possible to predict that radioactive isotopes will prove useful in the war against cancer, not in therapy, but rather in the field of biological discovery.

Chapter VI of the Cancer Commission Studies, "Sarcomas of Soft Tissues" by John Budd, M.D., will appear in this section in the October issue of CALIFORNIA MEDICINE.

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EDITORIALS

The Dodo Flies Again

With the adjournment of the 1947 California State Legislature, and more recently with the adjournment of the first session of the Eightieth Congress, word has been passed around in some medical circles that the issue of compulsory health insurance is as dead as a dodo. While such word is reassuring, we are beginning to wonder whether we should accept it as gospel.

A few recent incidents might serve to refresh our memories and to give us pause to consider whether or not compulsory health insurance has actually died. Possibly it has only gone to sleep, to awaken at a more propitious moment.

Consider, for instance, the action of the California State Federation of Labor (A. F. of L.) in circulating a statement before the Senate Subcommittee of the Committee on Labor and Welfare, a statement which branded the California Medical Association with asserted unconsciousness to public needs and disregard for sound social betterment.

Consider, again, the State Federation of Labor in writing to every member of the California State Legislature, to blast the C.M.A. for introducing a legislative bill which would ease the burden of selling voluntary health insurance by simplifying the selling process without depriving any individual of the right of self-determination. The State Federation of Labor calls this "compulsory health insurance" which it claims is a medical scheme to channel all voluntary health insurance into the hands of the doctors.

These items are in the record now and, after a one-day spell, out of the headlines. However, they are still in the minds of some legislators. Likewise in the legislative minds are memories of a recent labor blast against Senator Robert A. Taft of Ohio, who was accused in a labor convention of being anti-labor because he had opposed a health insurance program which the convention labeled as President Truman's but which we refer to as the Wagner-Murray-Dingell Bill. Senator Taft may be vulnerable to labor's attack on other grounds but this one is something new.

The final consideration is in the program of the California State Democratic Party, which has adopted health insurance as one of its goals. This has just happened and it means that every Democratic candidate in this state may be called upon by his party to espouse this brand of social soothing syrup.

The labor actions mentioned here might be expected as a part of labor's program of demanding its own way. But when these moves impinge upon the collective mind of the law-making bodies of the country, they represent political action. When they enter that stage, they represent a problem which organized medicine must meet if socialization of medical practice is to be avoided. Medicine has the weapons available to it to wage the fight needed; all it needs is the will to use these weapons. And if the medical soothsayers have their way, organized medicine would stack its weapons behind the door, to collect dust.

If the threat of socialized medicine is properly described in simile with the dodo, we strongly suspect that the ornithologists are misinformed as to the death of this bird.

Clinical-Pathological Conference*

A 36-year-old Filipino farm laborer was admitted to the Santa Barbara General Hospital with a complaint of pain in right chest.

Present Illness: The patient developed a severe "cold" four weeks before entering the hospital. This was accompanied by pain in the right side of his chest. As told by the patient, the cold was followed by pneumonia and he was admitted to another hospital because of high fever and productive cough. In that hospital he was treated with penicillin. A chest film taken at that time revealed a right pleural effusion. The fluid was aspirated with amelioration of the clinical symptoms. The temperature returned to normal but the productive cough persisted. Repeated examinations of the sputum were negative for tubercle bacilli and pathogenic fungi. Because tuberculosis was strongly suspected, the patient was transferred to the tuberculosis sanitarium at the Santa Barbara General Hospital. During this time he had lost 15 pounds.

Past History: The patient had always enjoyed good health and there was no pertinent medical or surgical history. He had been a resident of Santa Barbara County for the past 15 years, living in the Lompoc area. He had no knowledge of his diabetes prior to the hospital admission.

Family History: Father and mother deceased—cause of death not known. Three brothers were living and well.

Physical Examination: The patient was a fairly well developed, small Filipino. He was not in acute distress. There was no evidence of dyspnea. The only positive physical finding was diminished to absent breath sounds in the right lower chest posteriorly. The left chest was negative to percussion and auscultation.

Laboratory Findings: (On admission) Hb 14 grams. RBC 4,860,000; WBC 6,050; PMN 71 per cent; Lymphs 19 per cent; Eosins 10 per cent. Blood sedimentation rate, 11 mm. in one hour. Fasting blood sugar 296 mgm. per cent. Urine, albumin—trace, sugar—4 plus; Acetone and diacetic acid—negative. Serologic tests for syphilis, Kahn and Kline reactions—negative.

Radiologic examination of the chest on admission to the sanitarium revealed an area of increased density at the level of the left third rib posteriorly; the left lung parenchyma was radiographically clear. The right lung field showed evidence of cavitation at the level of the outer part of the second and third interspaces; there was a uniform dense shadow below this level which was suggestive of a fluid level.

Course in the Hospital: The patient was treated with diet and insulin therapy for control of the diabetes. After four weeks, urine sugar reactions were negative and the fasting blood sugar levels were below 100 mg. per cent. At this time 10 units of protamine zinc insulin were being given daily. His general condition appeared improved and he gained four pounds in two months. The chest symptoms completely subsided.

On July 30, 1946, approximately two months after admission to the Santa Barbara General Hospital, he began to complain of severe frontal headaches which were not associated with nasal discharge or sinus tenderness. Three 24-hour sputum specimens were examined at this time but no acid fast bacilli or other pathogenic microorganisms were seen. Chest films on July 31 showed only a small area of fibrosis at the level of the right second interspace and the radiologist suggested that if the chest lesions were caused by tuberculosis, the disease was probably in a healed state.

The headaches continued and required codeine for relief. A blood count on August 8, 1946, revealed WBC 13,500; PMN 64 per cent; Lymphs 21 per cent; Eosins 15 per cent. The patient became progressively more confused mentally and on August 12, a spinal tap was done. Pressure, 96 cm. of spinal fluid; Queckenstedt, negative. Spinal fluid sugar 57 per cent (blood sugar 190 mg. per cent). Cell count, WBC 605; PMN 10 per cent; Lymphs 90 per cent; RBC—too numerous to count. Globulin, "marked increase." Spinal fluid chlorides, 792 mg. per cent. Colloidal gold curve, 5555554331. Blood sedimentation rate, 34 mm. per hour.

The neurologic picture was not remarkable save for increasing mental retardation. The patient developed a marked tremor and urinary incontinence terminally. He expired quietly on August 18, 1946, three months after admission.

CLINICAL DISCUSSION

DR. HOBART A. REIMANN†: The case is one of about four months' duration, beginning with a "cold," followed by pleural effusion, pneumonia and cavitation of the lung. After a period of improvement and healing of the pulmonary lesion, evidence of intracranial disturbance developed about a month before death.

From the clinical records, tuberculosis was suspected, but the initial recovery was more rapid than one would expect if it had been tuberculosis pneumonia; tubercle bacilli were never found, there was

*One of three Clinical-Pathological Conferences held at the 76th Annual Session of the California Medical Association, April 30-May 3, Los Angeles.

†Professor of Medicine, Jefferson Medical College, Philadelphia.

eosinophilia and the sedimentation rate was not increased. If it were tuberculosis, the final state could have been interpreted as tuberculous meningitis or cerebral tuberculoma, but of which there was no diagnostic evidence. Fever is not mentioned after the early period in the description of the case, nor is the character of the sputum or the pleural effusion noted.

The history also suggests the possibility of viral pneumonia, followed, after too long an interval, however, by encephalitis. The pleural effusion, cavitation and eosinophilia do not favor this diagnosis.

Pulmonary abscess may have been considered because of the evidence of pneumonia followed by pleural effusion and cavitation. The cerebral symptoms could be explained by metastatic abscess in the brain. A "cold," on rare occasions, may give rise to lung abscess, but there is no evidence in the history of the aspiration of a foreign body or of surgical operation in the nose or throat. There is no description of the sputum or of the pleural fluid.

Carcinoma of the lung and metastasis to the brain is a possibility, but again, healing of the pulmonary lesion and other laboratory evidence does not favor the suggestion.

This leaves the most likely possibility to be discussed; namely, coccidioidomycosis with terminal coccidioidal invasion of the brain. The patient was a farmer who lived in an endemic area. The disease usually begins as a "cold" and in the great majority of cases never progresses beyond that brief period. In a few instances it causes more serious disease, as in the present one, probably abetted by the coexisting diabetes. Pneumonia indistinguishable from viral pneumonia occurs, but it is more often accompanied by pleural effusion and cavitation which, as described, may heal with little or no trace. In favor of this diagnosis are the patient's occupation, the clinical course, the normal sedimentation rate and a normal leukocyte count, with eosinophilia. No mention is made in the record of any specific tests for coccidioidomycosis.

It is well known that patients with coccidioidomycosis who do not have erythema nodosum during the initial stage are more likely later to develop the generalized form. In the present case, no skin lesions were noted, the pulmonary lesion healed, but one month later cerebral symptoms appeared which ended in death in another month. This suggests that infection persisted in the lung despite the negative roentgen ray evidence, and by way of blood stream the fungus eventually reached some area in the brain, probably the basilar region, lodged there and grew. Dissemination in some patients may include many organs and the brain is involved in 25 per cent of these instances. Furthermore, and as in the case at hand, localization may take place in the brain alone. A small percentage of persons who have had coccidioidomycosis even in its mildest form, especially those in whom no skin lesion occurred at the time, are liable to develop the disseminated form as long as ten years afterward.

The clinical diagnosis of the case is pulmonary coccidioidomycosis followed by coccidioidal basilar meningitis.

PATHOLOGIST'S DISCUSSION

DR. WILLIAM O. RUSSELL‡: When I heard that Dr. Reimann was discussing this case, I was reasonably sure that he would make the correct clinical diagnosis, knowing of his interest and experience with communicable diseases. There was one thing that was not given in the clinical history that would have further assisted Dr. Reimann in making the diagnosis of coccidioidomycosis. This was the fact that the patient lived in the Lompoc area in Santa Barbara County near Camp Cook. It was from Camp Cook that the first cases of coccidioidomycosis were reported in military installations in California during the war [1] and this area is now known to be endemic for this disease.

The postmortem examination of this man disclosed dense fibrous pleural adhesions over the surfaces of the lungs and sections of the lungs revealed small discrete white foci less than 1 mm. in diameter scattered in all of the lobes. A small cavity approximately 2 cm. in diameter was present in the upper lobe of the right lung. This cavity was surrounded by a small zone of moderately firm tissue and lined by a gray white caseous appearing surface.

In the mediastinum there were several enlarged lymph nodes having central caseous foci. Small gray white nodules similar to those seen in the lungs were noted in the liver, spleen and kidneys.

The weight of the brain was remarkably increased, being 1530 grams. The subarachnoid space over the base of the brain and particularly in the region of the optic chiasm was filled with a greenish yellow exudate. This exudate extended laterally into the sylvian fissures. Examination of the leptomeninges over the cerebral hemispheres disclosed small discrete yellow foci, most frequently seen in juxtaposition to the blood vessels in the sulci. Step sections through the brain disclosed moderate dilatation of the lateral, third and fourth ventricles. Small discrete slightly elevated nodules less than 1 mm. in diameter, imparting a fine granularity to the surface, were noted on the ventricular surfaces. In the vermis of the cerebellum, extending slightly into the right lobe, a focus of indurated tissue was noted that on section showed a large central area of caseous necrosis. The indurated tissue measured 13 mm. in diameter and involved the folia and the subarachnoid space.

I should like to admit at this time that, after reviewing these gross pathologic changes without the benefit of the microscopic examination, it was my opinion this was a typical case of tuberculosis with a cavity in the lung, with miliary dissemination to the lungs, liver, kidneys and spleen, and a tuberculoma in the cerebellum with leptomeningitis. However, I would like to add, apologetically, that at that time the clinical history was not available and I did not know of

‡Santa Barbara General Hospital, Santa Barbara, California.

the 10 per cent eosinophilia and that the patient lived in the Lompoc area.

Microscopic examination of the cavity in the upper lobe of the right lung, one of the enlarged lymph nodes in the mediastinum, the lesion in the cerebellum, the leptomeninges and the small gray foci in the parenchymatous organs disclosed in all instances granulomatous lesions containing spherules with double contoured capsules and frequently containing endospores characteristic of coccidioides immitis. Caseation was present but was remarkably different from what is usually seen with tuberculosis, there being a more acute type of inflammation with infiltrating polymorphonuclear leukocytes. A remarkable tendency was noted for the giant cells seen to have phagocytized the large spherules. The section taken from the cerebellum revealed the granuloma extending up to and involving the leptomeninges. This is a particularly significant fact in regard to the genesis of the leptomeningitis, since the question is posed whether the lesion in the cerebellum caused the meningitis or whether the subarachnoid space was infected from the blood. Certainly, in this case the leptomeninges could have been infected by organisms from the granuloma. It is interesting to note that, in the recently published studies of Forbus and Bestebreurtje,[2] the brain substance in coccidioidomycosis is not nearly so frequently involved as with tuberculosis. These authors concluded, therefore, that infection of the leptomeninges in coccidioidomycosis does not often result from the extension of a focus of the disease in the brain to the subarachnoid space. It was further pointed out that, because the organisms were of appropriate size to lodge within the vessels of the subarachnoid space, it was most likely that infection of the leptomeninges was by this means.

Anatomic Diagnoses: These were fibrocaseous coccidioidomycosis with cavitation in the upper lobe in the right lung; fibrocaseous coccidioidomycosis of the mediastinal lymph nodes; fibrous obliteration of the pleural cavities; miliary coccidioidomycosis of the lungs, liver, spleen and kidneys; coccidioidomycoma of the cerebellum; coccidioidomycotic leptomeningitis; granular coccidioidomycotic ependymitis; and internal hydrocephalus.

REFERENCES

1. Shelton, R. M.: Survey of coccidioidomycosis at Camp Roberts, California, J.A.M.A., 118:1186-1190 (April 4), 1942.

2. Forbus, W. D., and Bestebreurtje, A. M.: Coccidioidomycosis: a study of 95 cases of the disseminated type with special reference to the pathogenesis of the disease. The Military Surgeon, 99:653-719, 1946.

CLINICAL CONFERENCE

Psychosomatic Aspects of Migraine

FROM THE MEDICAL STAFF CONFERENCE, UNIVERSITY OF CALIFORNIA HOSPITAL, SAN FRANCISCO, MARCH 26, 1947

DR. PAUL A. GLIEBE *: This morning we plan to discuss the psychosomatic aspects of allergic disorders. Since we have available for presentation a man who has suffered from migraine, we will restrict our discussion to this problem and to the general subject of headaches. It is common knowledge, of course, that distressing emotional situations not infrequently "give one a pain in the neck, or are enough to give one a headache;" yet because this is a truism we overlook or under-rate the importance of the emotional elements in any physical complaint. The patient to be presented has been investigated thoroughly from every physical viewpoint; the sole conclusion was a diagnosis of migraine.

CASE PRESENTATION BY DR. ALFRED AUERBACK †: Mr. S. is a 40 year old lawyer. He was troubled by typical migraine headaches for nearly 23 years. Will you describe your headaches, Mr. S.?

MR. S.: They always began with distortion of vision, similar to the turning of a windmill wheel, occurring at the side of the eyes. This developed to the point where my vision was practically nil. This was followed by very severe headache with pain extending into the neck and shoulder. The headaches were accompanied by nausea and vomiting. I could not stand light. I went to bed in a darkened room for eight to twenty-four hours. It took another day to come back to normal.

DR. AUERBACK: How long and how frequently did you have headaches?

MR. S.: From once a week to twice a year for 22 to 23 years..

DR. AUERBACK: How long is it since you have seen me?

MR. S.: October 1944.

DR. AUERBACK: How many migraine headaches have you had since then?

MR. S.: None.

DR. AUERBACK: How do you account for it? Would you tell the doctors very briefly why you had migraine headaches?

MR. S.: I was a breech birth baby, causing an injury to my mother. When I was around ten or twelve years old, she had an operation to correct this injury. Someone in the family—I don't remember who—informed me why she was having the operation. That made quite an impression on me to think that I had been responsible for her having this operation. That operation, in turn, resulted in a hernia. She had two subsequent operations to correct the hernia, neither of which were successful. And all her life she has been suffering from that. In my interviews with you, I discovered that I was suffering from feelings of guilt, blaming myself for her ill health.

DR. AUERBACK: Did any one else in your family have migraine?

MR. S.: My mother did. I don't know about any other member of my family.

DR. AUERBACK: What Mr. S. has told you about his feelings of guilt and responsibility for his mother's illness constitute a very important factor in the production of his migraine attacks. However, the background underlying the production of migraine headaches is more complicated; he did not mention the tremendous hostility he has had toward his mother all through life. His mother was the dominant person in the household, managing the father, and profoundly influencing the lives of her children. She was opposed to her son's going with girls or getting married. She did everything in her power to prevent the patient going with girls during the time he was in high school. This was the cause of repeated arguments between the patient and his mother, arguments the mother invariably won.

Another source of conflict was the fact that the patient wanted to go to college, and the mother continuously opposed this for financial reasons. The patient developed terrific resentment toward his mother, but owing to her continuous ill health, for which he felt largely responsible, he did not voice his difference of opinion very frequently, and when he did he had a profound feeling of guilt.

Mr. S. always thought he was his mother's favorite, and recalled at a very early age identifying with her. Identification with his mother was reinforced by the fact that all his life he had felt physically inferior to his father and brothers. From early infancy the patient had found that any illness brought him considerable attention from his mother and family, and made him a very important person in the household: "All my life I had the idea that I should have something wrong with me. My headaches came on during my adolescence when my mother was having her recurrent operations for the birth injury which I felt was my fault. In addition, I was having considerable conflict with her over the fact that I wished to go with girls, and she strongly opposed it; also, that I was very desirous of going to college and she opposed

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this too. Whenever I stood up to her or criticized her, I felt very guilty. It was in this setting of mixed emotions, of resentment and guilt, that seemingly I extended my identification with my mother to acquiring a migraine headache similar to those she suffered."

Wolff states that 90 per cent of headaches arise from emotional tension. Friedman, Brenner and Merritt have concluded also that the majority of patients with chronic headaches have these arising from emotional stress and inner conflicts. It is their feeling that psychotherapy is every bit as important as drug therapy, and that simple psychotherapy, such as is within the province of the general practitioner, often is very effective therapeutically. It is surprising, considering how frequent headaches are, how little has been written on this condition. Recent reports describe migrainous patients as sensitive, reserved, repressed individuals who have considerable anger that they hold tightly in check. Unable to give vent to their feelings, they symbolically "blow their tops." Our patient reported that on one occasion when he was suffering a very severe migrainous headache, he asked a nurse for an injection of Gynergen which was refused him. He became so enraged at the nurse he "bawled her out," and was amazed to find that his headache practically disappeared.

Psychotherapy employed in this case is similar to that used in all cases that come to a psychiatrist's attention. The life history is reviewed, finding out specific incidents in childhood and later life which could give rise to patterns of instability, followed by a detailed discussion of immature and mature methods of reacting to these situations. It is pointed out to the patient that rather than reacting emotionally to frustrations, he must realistically face the situation; that is to weigh the possible solutions and decide which is best for the particular situation. By learning to think and consciously changing his pattern of reaction, he can develop a more healthful pattern for coping with the problems that arise in life. In developing an attitude of seeing things objectively and realistically, feelings of hostility, guilt and inferiority soon disappear. In psychiatric practice we have found that if patients are able to verbalize their hostilities, their headaches are immeasurably improved. In the case of Mr. S., our discussions served to relieve him of his feeling of guilt for his mother's chronic illness. He was able to admit to himself the resentment he had towards his mother, and by talking it out in my office, has been able to effect a better relationship with his mother than at any time before in his life. He can now visit his mother without developing any symtoms whatever, and is no longer disturbed by any of her domineering attitudes toward him.

DR. CHARLES ARING‡: I don't suppose there is any one here who knows any more about the mechanisms of the central nervous system than I do. I know where the cells lie, where the tracts run, about conduction, about the axone reflex and triple response. I know approximately what any other expert on neurology knows about mechanism. Yet, this is of no use whatsoever in the therapy of such a patient as we have just seen. One could handle this case just as well if he knew nothing about mechanism. This case illustrates how the physician and patient may be in conflict. The doctor wants to know about mechanism, what the physiochemical distortions are. The patient wants relief. He is not in pursuit of the ideal of health in any direct sense.

A psychosomatic affection has been defined as a bodily disorder, the nature of which can be appreciated only when emotional disturbances are investigated in addition to physical disturbances. One must know what kind of person the patient was before he became ill. Why did he get sick when he did? Why did he get sick in the manner that he did? These questions may be answered in many cases if you will allow the patient to talk without too much interruption.

The question of heredity in migraine merits consideration. I do not imply that it is genetically inherited. I find no difficulty believing that parents may subtly transfer to the child their methods of living or. in other words, their social techniques. One frequently hears of migraine in a long line of forebears. It is imperative to break this chain lest the Biblical admonition come true, "The sins of the father shall be visited upon the third and fourth generations."

‡Professor of Neurology, University of California Medical School, San Francisco. (Since resigned)

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NOTICES AND REPORTS

The A.M.A. Centennial

Report of the Chairman of the C.M.A. Delegation

JOHN W. CLINE, M.D., *San Francisco*

The Centennial of the American Medical Association held in Atlantic City in June was notable for the large attendance, the number of foreign guests and the quality and diversity of the scientific programs. Practically every country was represented and the attendance was said to total over 15,000.

The House of Delegates was in practically continuous session throughout the four days and its deliberations covered a wide range of subjects. The major portion of the time was devoted to the problems of the general practitioner, certain of the economic phases of medicine and the public relations program of the A.M.A.

Concern was expressed over the current tendency of young doctors to seek specialist training and recognition and to shun general practice. Efforts were made to induce hospitals to be less restrictive in granting staff memberships and the Council on Medical Education and Hospitals was instructed to revise the rules for approval of hospitals for resident training so that requirements of experience and proficiency would replace board certification and membership in special societies for staff membership.

At the December, 1945, meeting, interim sessions of the House of Delegates were established. It was decided at this meeting to hold these meetings in different parts of the country each year and to hold two-day scientific meetings devoted to the needs of the general practitioner in conjunction with them.

A committee was established to survey current medical education, to ascertain methods of utilization of hospitals to train general practitioners, and to investigate the adequacy of numbers and distribution of physicians. This action was designed to ascertain facts in an effort to improve the situation of general practice.

The stand of the American Medical Association in opposition to socialization of medicine was reiterated and voluntary plans were encouraged. The Association of Medical Care Plans is to be given greater assistance. The Bureau of Medical Economics is to be expanded.

There were many other items of medico-economic importance considered, including study and formulation of a code covering group practice, the nursing shortage, fees paid by government agencies, and pay for physicians in service.

The public relations program of the A.M.A. started in San Francisco last year came to a standstill at this meeting due to an impasse reached by the Board of Trustees and the Public Relations Advisor and the Executive Assistant in charge of Public Relations. There were a number of factors in the development of this situation which culminated in the resignation of the Advisor and the Executive Assistant. This temporarily leaves the A.M.A. without professional public relations aid. The House of Delegates decided that the office of Executive Assistant is to be filled as promptly as possible, and in the interim public relations will be under the direction of the Executive Committee of the Board of Trustees. The Board has expressed a determination to see that the public relations of the A.M.A. are adequately handled but has not yet had time to make the necessary appointment.

The California resolution regarding public relations was passed with little change. The California delegation was well represented on reference committees and was active in the deliberations of the House.

Dr. Dwight Murray of Napa was reelected to the Board of Trustees by an overwhelming majority.

C.P.S. Enrolls Employees Of Standard Oil

California Physicians' Service has recently completed the enrollment of the employees of Standard Oil Company of California and its designated subsidiaries. Over 6,800 employees of the Standard Oil Company joined C.P.S. during the drive, and the final tally showed that (including family dependents) over 15,000 new members were enrolled in this one statewide campaign.

This latest large-scale enrollment effort is noteworthy for two reasons:

1. Since Standard Oil Co. is one of the State's key industrial groups, its acceptance of the C.P.S. program marks a high point in the development of prepaid voluntary medical service.

2. The enrollment effort was carried out in direct competition with one of the country's leading insurance companies, offering fine indemnity type contract. Enrollment proceedings were carried out in such a way as to allow a direct comparison in public desire in the health insurance field. Medical service at a slightly higher cost, or indemnity at a lower cost?

The results were astonishing. Medical service won with a preference shown of better than two to one. Over 6,800 applications for C.P.S. service were received, while only 3,300 applications were turned in requesting the insurance indemnity plan.

The circumstances surrounding the enrollment of this group are probably the most unusual that C.P.S. has encountered to date. Standard Oil Co. felt that its employees should have the opportunity to study both types of coverage and then voluntarily choose the plan which they felt would be of the most service to them. A special packet, containing specially prepared and censored sales literature, explaining both Programs, was distributed under Standard Oil sponsorship, to all employees throughout the entire State. At the same time, notification was given of special meetings to be held on company property and on company time, with the request that all employees attend. Representatives of both the insurance company and C.P.S. were given equal time to explain their respective programs. A specially appointed Standard Oil Co. official was on hand at every meeting to act as moderator and to explain the company's reasons for the proceedings. The last half of each meeting was devoted to a question and answer period and the employees in attendance were urged to direct questions to either or both of the representatives. All sales presentations were limited to factual material, with no direct comparisons allowed.

The basic issues were simple and to the point: Does indemnity answer your personal needs? Does medical service answer your requirements more to your satisfaction?

The final results were so positive that very little doubt can remain in the minds of the proponents of either method.

Several very interesting facts were turned up during the campaign. The newly formed C.P.S. Industrial Relations Department was called into action and the results bear special mention. The C.I.O. Oil Workers Union in Richmond, endorsed the C.P.S. program and the enrollment results in that area were highly successful.

Family participation in this Standard Oil Group was unusually high with an average of 2.5 per cent participation per application, as against a statewide average in all other groups of 1.95 per cent.

The total percentage of enrollment, including both contracts, was 61.2 per cent. Future reopenings of the group will, without a doubt, increase the percentage of participation materially.

The successful enrollment of organizations of the caliber of Standard Oil of California are continually increasing the prestige of prepaid medical service as the best answer to the public demand for protection from the economic shock of medical, surgical and hospital care.

Requests for Cancer Manual

Close to half the members of the California Medical Association have asked that they be sent the bound volume of articles in the California Cancer Commission Studies which is to be made up some two years hence, after each of the chapters in the studies has appeared in CALIFORNIA MEDICINE. Intended to aid the practicing physician in the diagnosis and management of early cancer, the manual is to be supplied free of charge to California Medical Association members requesting it.

To determine the number of bound volumes needed, the Cancer Commission early in July sent returnable postcards to all members, asking that they indicate whether they wished to receive the manual. By mid-August some 4,200 of the cards had been returned. Few of the physicians who returned cards said that they did not wish to receive the manual. Some of the cards did not indicate whether the sender did or did not want the bound volume, but in such cases the Cancer Commission will send the manual. Several of those who returned cards asking for the volume neglected to sign their names, so that it is not known where to send the book when it is completed.

Refresher Course on Cancer

The California Cancer Commission announces the second Refresher Course on Cancer for physicians to be held in Los Angeles County General Hospital on Sunday and Monday, October 5 and 6. This course, like the one in January, will be under the supervision of the Tumor Board of the Los Angeles County General Hospital and the expenses of the course will be underwritten by the California Division of the American Cancer Society.

The program has been prepared by a sub-committee of the Cancer Commission consisting of Dr. George Sharp and Dr. Clarence Berne. Instructors

have been selected from the faculties of the University of Southern California School of Medicine and the College of Medical Evangelists, and from the Los Angeles County Medical Society.

Through the support of the California Division this two-day course is offered without charge to practicing physicians in southern California. Because of limited facilities, reservations should be made immediately with Dr. E. M. Butt, 1200 North State Street, Los Angeles 33.

October 5, 1947

AFTERNOON

ERIC LARSON, M.D., *Chairman*

1:00-1:15—Welcome by Cancer Commission.....Lyell C. Kinney, M.D.
Welcome by Los Angeles County Hospital Tumor Board.....H. P. Jacobson, M.D.
1:15-2:00—General Tumor Pathology.....A. G. Foord, M.D.
2:10-2:40—Historical Development of the Cancer Problem.....Ian Macdonald, M.D.
2:40-3:10—Management of Melanoma....John W. Budd, M.D.
3:20-4:00—Skin Cancer Treated by General Surgery.....C. H. McIntyre, M.D., Leo Kaplan, M.D.
4:00-4:30—The Legal Responsibility of the Physician to Neoplastic Disease.....Louis J. Regan, M.D.

EVENING

WM. E. COSTOLOW, M.D., *Chairman*

8:00-8:30—Experimental Cancer Research.....H. E. Pearson, M.D.
8:30-9:00—Biochemistry of Growth.....H. J. Duel, M.D.
9:10-9:30—Malignant Tumors of Bone.....Frances M. McKeever, M.D.
9:30-10:00—Management of Uterine Bleeding.....Erle Henricksen, M.D.

October 6, 1947

AFTERNOON

H. P. JACOBSON, M.D., *Chairman*

1:00 2:00—Tumor Board Meeting. Presentation of Cases.
2:10-2:40—Diagnosis of Pulmonary Neoplasms.....Reginald Smart, M.D.
2:40-3:10—Tumors of the Oral Cavity..George S. Sharp, M.D.
3:20—Differential Diagnosis of Tumors of the Neck.....C. J. Baumgartner, M.D.
3:50-4:30—Psychology of Management of Cancer Patient.....Chas. A. Sturdevant, M.D.

EVENING

LEROY B. SHERRY, M.D., *Chairman*

8:00-8:30—Roentgenologic Diagnosis of Gastro-Intestinal Tumors.....Kenneth S. Davis, M.D.
8:30-9:00—Benign Tumors of Bone..Paul S. McMaster, M.D.
9:10—Biopsy and Pathology of Cancer of Breast.....Louisa B. Keasby, M.D.
9:40—Diagnosis and Treatment of Cancer of Breast.....C. J. Berne, M.D.

In Memoriam

BETTS, IRVIN H. Died in San Francisco, July 1, 1947, age 58, following a year's illness with heart disease. Graduate of the University of California Medical School, Berkeley-San Francisco, 1915. Licensed in California in 1915. Dr. Betts was a retired member of the Tulare County Medical Society, the California Medical Association, and an Affiliate Fellow of the American Medical Association.

HUFF, EDMUND NEWELL. Died in South Pasadena, July 3, 1947, age 69, of aortic aneurysm (arteriosclerotic) chronic hypertension. Graduate of the Hahnemann Medical College and Hospital of Philadelphia, Pennsylvania, 1900. Licensed in California in 1939. Dr. Huff was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

MCKENNA, STEPHEN EUGENE. Died in Los Angeles, June 16, 1947, aged 37, of bulbar poliomyelitis. Graduate of the University of California Medical School, Berkeley-San Francisco, 1937. Licensed in California in 1937. Dr. McKenna was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

MACNAMARA, GEORGE A. Died in National City, July 3, 1947, age 51, of heart disease. Graduate of New York University College of Medicine, New York, 1931. Licensed in California in 1942. Dr. MacNamara was a member of the San Diego County Medical Society, the California Medical Association and a Fellow of the American Medical Association.

MURPHY, JAMES EDWARD. Died in Sacramento, May 17, 1947, age 54, of myocardial infarction. Graduate of St. Louis University School of Medicine, Missouri, 1923. Licensed in California in 1924. Dr. Murphy was a member of the Sacramento Society for Medical Improvement, the California Medical Association, and a Fellow of the American Medical Association.

NEWS and NOTES

NATIONAL • STATE • COUNTY

LOS ANGELES

The **Medical Veterans Association** of Los Angeles held its first annual stag banquet at the Los Angeles Breakfast Club, July 24. Approximately 400 physicians attended and a number of dentists were also present. Many acquaintances were renewed and there was a great deal of reminiscing about experiences while in the service. One of the features of the evening was a brief address by E. T. Remmen, M.D., president of the Los Angeles County Medical Association. Many new members were enrolled and an invitation to join the Association was extended to all medical, dental and nursing officers, veterans of World War II, who served with either the United States or Allied Forces. Other social events are being planned for the future and an invitation will be extended to all those eligible to membership to attend.

Dr. Sherman Miller, who has been practicing medicine from his home for several months since his discharge from the Army, has announced the opening of an office in Culver City.

SAN BERNARDINO

Dr. F. E. Wiggins has replaced Dr. Frank M. Gardner as the health officer of the city of San Bernardino.

SAN DIEGO

Dr. J. B. Askew, Chief of the Bureau of Hospital Inspections since it first began operation in January of 1946, has resigned from the staff of the State Health Department to become the assistant health officer of San Diego County. Dr. Askew will serve under **Dr. Alex Lassen,** San Diego County Health Officer.

Dr. Sam J. McClendon, San Diego, a member of the State Board of Public Health and past president of the California Medical Association, was elected president of the California Heart Association at its annual meeting in Los Angeles recently.

SAN FRANCISCO

Asked by the United Nations to help set up the National Neuropsychiatric Institute of Nanking under the auspices of the World Health Organization, **Dr. Karl Bowman,** medical superintendent of the Langley Porter Clinic in San Francisco, has flown to China where he is scheduled to spend three months on the project. It is planned to make the Nanking Institute a training center and focus of teaching and research in psychiatry for all China.

SAN JOAQUIN

Recently discharged from the army, **Dr. Arnold A. Michals** has joined his father, Dr. N. J. Michals, in the practice of medicine in Lodi. The younger Dr. Michals will specialize in surgery.

SAN LUIS OBISPO

Dr. Philip A. Bearg has resigned as health officer of San Luis Obispo County. As yet no one has been appointed to fill the vacancy.

SAN MATEO

Appointment of **Dr. J. C. Shrader** and **Dr. Francis E. Howard** to the staff of the Redwood City Clinic has been announced by the clinic. Dr. Shrader, an internist, recently received his discharge from the Army after four years' service. Dr. Howard has been chief resident surgeon at Community Hospital in San Mateo, a post he had occupied for 15 months following discharge from the Navy.

Announcement has been made of an association of six physicians, five of them veterans of World War II, to form the **Menlo Medical Center** in Menlo Park. They are Dr. Ernest H. Sultan, general practitioner; Dr. Frederic P. Schidler, surgeon; Dr. Charles D. Armstrong, internist; Dr. Gordon E. Williams, pediatrician; Dr. Peter S. Talbot, obstetrician and gynecologist; and Dr. Stanford B. Rossiter, radiologist. Plans are to construct a building to house the center in Menlo Park. It is expected to be ready for occupancy by March of next year.

STANISLAUS

Dr. H. L. Archibald, upon completion of his terminal leave from the Army, has become associated with Dr. E. G. Allen with offices in Patterson.

GENERAL

Dr. G. H. A. Clowes, Ph.D., Sc.D., LL.D., director emeritus of the Lilly Research Laboratories, was honored by the American Diabetes Association at its recent annual meeting in Atlantic City, New Jersey. He delivered the annual Banting Memorial address and was awarded the Banting Medal which is given in recognition of distinguished service in the field of diabetes. Under Dr. Clowes' direction, the Lilly Research Laboratories cooperated with the University of Toronto and Drs. Banting and Best in the early development of insulin of sufficient purity and stability to permit its widespread clinical use throughout the world.

An organization of nearly 100 doctors which several months ago was formed as a labor union called the Association of Santa Fe Coast Line Physicians, is negotiating with the Santa Fe Hospital board of trustees on wages, rules and working conditions, according to a report by International News Service.

Demand that the Department of Justice take steps to stop six government agencies from spending government money for "propaganda promoting socialized medicine" is being pressed by Representative Harness (R., Indiana). Representative Harness, who is chairman of a House investigating committee, has asked an investigation of the U. S. Public Health Service, the Office of Education, the Children's Bureau, the U. S. Employment Service, the Department of Agriculture and the Bureau of Research and Statistics. The committee he heads has charged in its findings that all the six agencies named were "known to have participated in the socialized medicine campaign." The report said that key personnel in the agencies had set up health workshops in strategic areas "to build up an artificial, federally stimulated public demand upon Congress for enactment of the Wagner-Murray-Dingell bill providing compulsory health insurance."

Organization of an affiliated "eye bank" in New Orleans has been announced by the Eye-Bank for Sight Restoration, Inc. The new eye bank, the third affiliate to be formed, will operate in cooperation with the Louisiana State University Medical School and the Tulane University Medical School and Hospital. Other affiliated eye banks are functioning in Boston and Chicago.

The American College of Physicians will conduct its 29th Annual Session at San Francisco, April 19-23, 1948. General headquarters will be at the Civic Auditorium. **Dr. William J. Kerr** and **Dr. Ernest H. Falconer**, both of San Francisco, are the co-chairmen for local arrangements and the program of clinics and panel discussions. The president of the college, **Dr. Hugh J. Morgan**, Professor of Medicine at Vanderbilt University School of Medicine, Nashville, Tennessee, is in charge of the program of morning lectures and afternoon general sessions.

The Office of Military Government for Germany (U. S.) has a position vacancy in its Public Health and Welfare Division for a qualified physician to serve as Public Health Officer at Bremmerhaven, Germany, at a salary of $8,877.75 a year. Full details and a description of the duties may be had from Major D. Donald Klous, War Department Special Staff, Civil Affairs Division, Personnel and Training Branch, Washington 25, D. C.

More than 1,000 medical specialists in x-ray and radium are expected to attend the 48th annual meeting of the American Roentgen Ray Society which will be held at Haddon Hall in Atlantic City, September 16-19, according to an announcement by the society.

Recommendation for "the establishment of departments of Anesthesiology in all medical schools and hospitals under the direction of a doctor of medicine actively engaged in the practice of Anesthesiology," was made in a resolution by the American Society of Anesthesiology in a resolution adopted by its Board of Directors at a meeting in Atlantic City, June 11. The resolution recommended that "the department of Anesthesiology shall bear the same relationship to the medical school and/or hospital as is borne by other medical departments of the institution."

In the same resolution the society went on record as disapproving of "the training of persons other than doctors of medicine in the science and art of anesthesia, for the assumption of responsibility in the care of patients where it may be necessary to exercise medical judgment, and particularly does it disapprove of the issuance of certificates for such training by its members."

It further disapproved "the existence of departments of Anesthesiology in hospitals and/or medical schools under the direction of persons other than doctors of medicine or under the nominal direction of doctors of medicine not actively engaged in the practice of Anesthesiology."

Acting for the **American Cancer Society**, the Committee on Growth of National Research Council announces that it is ready to receive **applications for fellowships and grants** in cancer research for 1948. October 1 is the deadline for receipt of applications to extend existing grants and November 1 for new grants. Requests for fellowships and senior fellowships in cancer research may be submitted as late as December 1. Communications should be addressed to Executive Secretary, Committee on Growth, National Research Council, 2101 Constitution Avenue, Washington 25, D. C. Final decisions on applications will be made in February. Ordinarily, the grants and fellowships become effective in July.

"During the past two years," says the announcement, "the American Cancer Society, acting upon the recommendation of the Committee on Growth, has awarded 176 grants and 47 fellowships representing a total expenditure of some $2,700,000. The Committee will continue to recommend support of biological and clinical research dealing broadly with phenomena relating to growth, typical or neoplastic. In the formulation of this program the committee will be guided, as in the past, by the advice of some 120 scientists grouped in 20 panels comprising its sections on biology, chemistry, physics, chemotherapy, clinical investigations and fellowships."

INFORMATION

Public Relations and the Bureau of Medical Economics

ROLLEN WATERSON *

Common sense points the way to good public relations for medicine. The primary requirement is that the individuals who comprise medicine—all physicians—earn good relations with the individuals who comprise the public—all patients.

Public relations is an art that must be practiced *by* doctors of medicine. Contrary to popular belief, it can not be practiced *for* medicine by employed experts—the spellbinder, the press agent, the propagandist.

Medicine's public relations—good or bad—is the end product of each contact between physician and patient. Public relations, therefore, becomes synonymous with *human* relations.

This basic public relations concept was the force leading to the establishment of the Bureau of Medical Economics by the physicians of Alameda County. The Bureau's purpose is to serve as a coordinating agency for doctors' efforts to remove barriers preventing complete economic understanding with their patients.

Misunderstandings—which add up to bad public relations—must often find expression in the patient's failure or refusal to pay for the doctor's services.

Judged by sordid statistics supplied by a study of the nation's commercial collection agencies, the known proportion of disgruntled patients to satisfied ones is in itself alarming. From one-fourth to one-third of the families in most cities in the nation have been hounded at one time or another by collectors for doctor bills.

There is no way of estimating the additional unknown number who escape this category by settling their medical accounts without coercion but with the vow that "I'll never go to *that* doctor again!" Together these groups form a bloc which is medicine's biggest obstacle to good public relations. The bloc was created by individual doctors; it can be removed only by individual doctors.

It is a fact that in most communities, bill collectors handle a greater dollar-volume of accounts for physicians *than for all other credit grantors combined.* Delinquent medical accounts form the only factor in the economic life of a community which can be and often is the sole support of a commercial collection agency. If this much economic difficulty with its customers became true of any commercial enterprise it would mean failure for that enterprise. If this continues to be true of medicine, it will mean the usurpation of the economics of medicine by those who proffer the promise of better business management—the government, the insurance companies, the hospitals.

Cure for these maladjustments and prevention of them is the province of the Bureau of Medical Economics.

The *cure* is being achieved by the individual arbitration of existing economic differences as represented by delinquent accounts. *Prevention* is being accomplished by applying, to the individual doctor's practice, sound medical business methods developed through Bureau research.

The Bureau supplants the commercial bill collector as medicine's chief ambassador of public relations. In its role as liaison between physician and patient, the physician-owned and -operated Bureau approaches each unpaid account problem from the standpoint of medical ethics and ideals: Will full payment of this bill work undue hardship on the payor?

Investigation has proved that persons who are delinquent in payment of doctor bills fall into three main categories: those on whom payment would work a genuine hardship; those who have failed to pay because of a genuine misunderstanding; and those who just have a genuine desire not to pay, period.

In the first group an adjustment is recommended to the doctor by the Bureau. (Actually less than one per cent need to be adjusted). In the second, the reason for the misunderstanding is determined and removed. In the third—then, and only then, are strong collection methods put into effect—*effectively.*

Paradoxically, this humane treatment produces greater return for the doctor at a lower rate of collection commission than was possible under the old system of commercial collector ruthlessness. At the same time there is a parallel achievement in that it is earning good public relations for medicine as a whole.

Bureau employees have made personal contact with more than one hundred thousand patients who have not paid their doctors. This broad experience provides a category for virtually every reason for patient dissatisfaction and delinquency. Through the other work of the Bureau, much has been learned of the manner in which one doctor builds satisfaction—and his practice—while another doctor unwittingly is destorying these very things.

This body of information is being carefully compiled and correlated. From it doctors are learning more and more how the business aspect of their offices must be conducted to achieve satisfaction in each physician-patient relationship. This results in a financially better practice for the doctor—and better public relations for medicine.

* Executive Secretary, Alameda County Medical Association.

An incidental sidelight on the program is offered by the Alameda County Medical Association, the Bureau having made it possible to advertise the fact that no one in the county need go without medical care because of inability to pay. The Association advertised for that individual who could not obtain medical care because he could not pay for it. No such person was found. But had medically-needy persons been found, medicine was organized, through the Bureau, to satisfy their needs.

Specific services provided by the Bureau of Medical Economics include:

For the doctor—
- Medical office management advice
- Collections
- Auditing
- Accounting
- Bookkeeping
- Statement preparation and mailing
- Investigation of patients' ability to pay
- Credit reporting
- Delinquency prevention
- Tax advice
- Malpractice prevention

For the patient—
- Ethical collection of delinquencies
- Adjustment of fees to ability to pay
- Fee complaint consideration (by medical association committee)
- Financing of medical costs
- Postpayment of medical costs
- Medical social service
- Information and advice on health insurance

Medicine cannot avoid being the target for attack from politicians, demagogues and crackpots so long as its public relations problems remain acute. The Bureau of Medical Economics alone will not solve these problems. Other important work must be and is being done by county and state medical societies. But until the objectives of the Bureau's program in human relations are reached, no amount of effort in other channels will achieve the desired over-all result.

There *must* be widespread improvement in the individual physician-patient economic relationship. This is being accomplished through the Bureau of Medical Economics, medical societies and physicians of the San Francisco Bay Area counties of Alameda, San Francisco, and Santa Clara, where offices of the Bureau are established and operating.

Distribution of Physicians in California in Relation to Population Shown by C.M.A. Survey

The California Medical Association is consulted frequently regarding possible openings for private practice in this state. In order to be able to inform inquirers as to the locations in greatest need of physicians, a study was made during the last several months of the geographic distribution of practicing physicians and of the feasibility of developing a map showing "Medical Service Areas."

The following table shows the general statewide picture:

Year	Population	C.M.A. Members	Other M.D.s*
1940	6,907,400	6,349	4,241
1947	9,420,000	8,605	4,480

* These include many retired physicians, some physicians in full-time educational and industrial positions and some not eligible for membership in the C.M.A.

The map (see Figure 1) shows the physician distribution by counties as of July, 1947. The unshaded areas (five counties) are those with one physician, M.D., per 1,000 persons or less; the dotted areas, those with one physician per 1,000 or 1,500 persons; the striped areas, those with one physician per 1,500 to 3,000 persons, and the cross hatched areas (only four counties) those with one physician per 3,000 persons or over.

There are no counties in California lacking a physician. There are some geographical areas in which physicians are few and it is to these areas that a majority of our inquirers are urged to direct their attention.

A protracted attempt was made to create a "medical service area map," that is, a map showing groups of counties or portions of counties which could be regarded as an area in which medical service was furnished from a given center. Because of the frequent overlap between different medical service areas, it was not possible to develop such a chart.

An "Advisory Committee on Hospital Facilities" has recently issued tentative proposals for medical service areas grouped around hospital facilities actually present or to be constructed. The committee divided the state into 16 hospital regions as follows:

PROPOSED HOSPITAL REGIONS IN CALIFORNIA

Region 1.—Regional Hospital: Redding; Community Hospitals or Service Centers: Yreka, Alturas, Dunsmuir, Tulelake, Cedarville, Adin, Bieber and Weaverville.

Region 2.—Regional Hospital: Eureka; Community Hospitals or Service Centers: Crescent City, Fortuna and Garberville.

Region 3.—Regional Hospital; Chico; Community Hospitals or Service Centers: Red Bluff, Westwood, Oroville, Willows, Gridley, Portola and Quincy.

Region 4.—Regional Hospital: Sacramento; Community Hospitals or Service Centers: Woodland, Placerville, Auburn,

Grass Valley, Marysville, Arbuckle, Roseville, Downieville, Truckee, Jackson and Colusa.

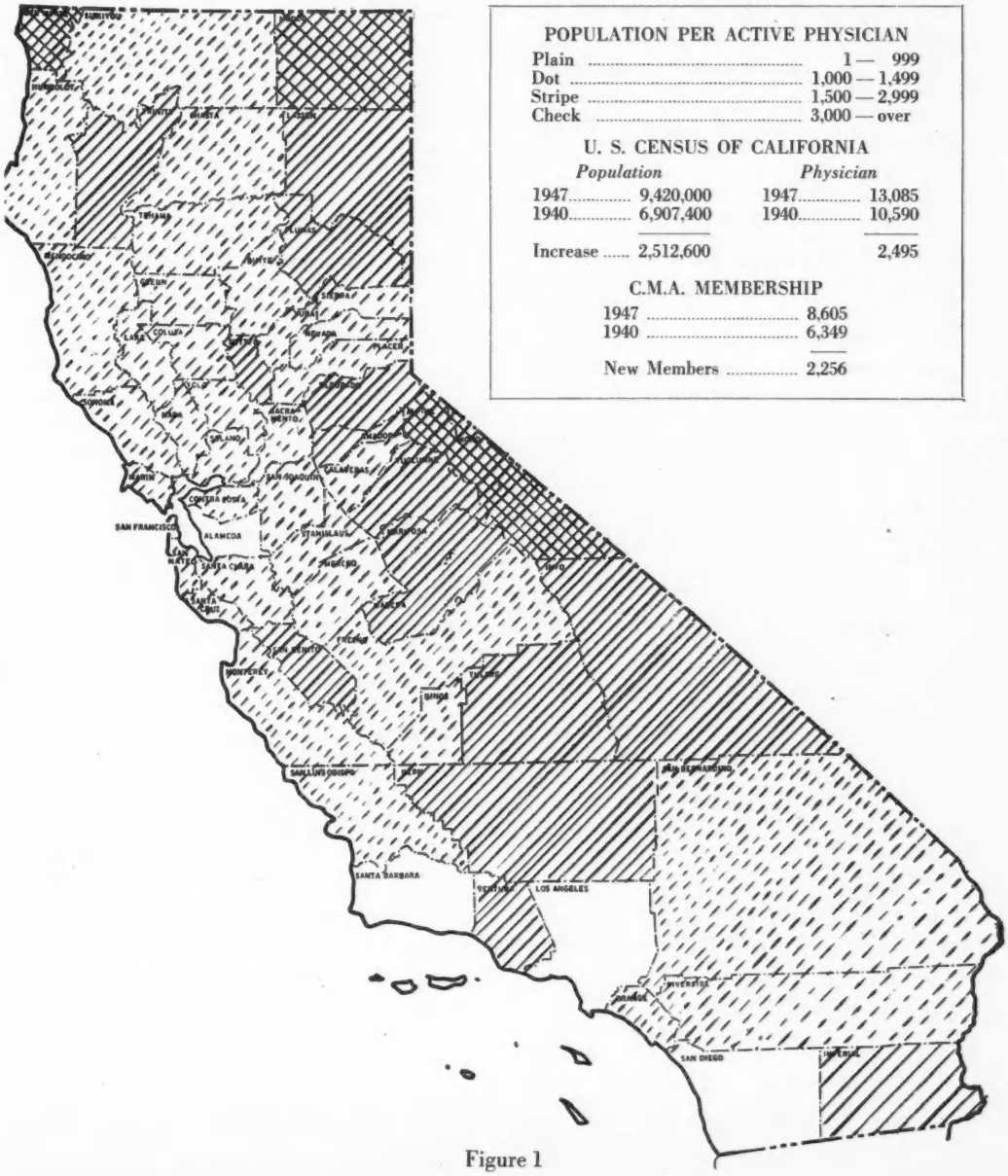
Region 5.—Regional Hospital: Santa Rosa; Community Hospitals or Service Centers: Fort Bragg, Lakeport, Napa, Ukiah, Willits, Healdsburg, Calistoga and Petaluma.

Region 6.—Regional Hospital: Oakland; Community Hospitals or Service Centers: Berkeley, Alameda, Vallejo, Pittsburg, Martinez, Richmond, Concord, Fairfield, Hayward, Livermore and Antioch.

Region 7.—Regional Hospital: Stockton; Community Hospitals or Service Centers: Lodi, Tracy, Modesto, Sonora, San Andreas, Patterson, Oakdale, Los Banos, Mariposa, Markleeville, Merced, Turlock and Yosemite.

Region 8.—Regional Hospital, and Teaching Center: San Francisco; Community Hospitals or Service Centers: San Rafael, South San Francisco, San Mateo and Redwood City.

Region 9.—Regional Hospital: San Jose; Community Hospitals or Service Centers: Palo Alto, Watsonville, Santa



POPULATION PER ACTIVE PHYSICIAN

Plain	1 — 999
Dot	1,000 — 1,499
Stripe	1,500 — 2,999
Check	3,000 — over

U. S. CENSUS OF CALIFORNIA

Population		*Physician*	
1947	9,420,000	1947	13,085
1940	6,907,400	1940	10,590
Increase	2,512,600		2,495

C.M.A. MEMBERSHIP

1947	8,605
1940	6,349
New Members	2,256

Figure 1

Cruz, Santa Clara, Los Gatos, Gilroy and Centerville.

Region 10.—Regional Hospital: Fresno; Community Hospitals or Service Centers: Madera, Selma, Hanford, Visalia, Tulare, Porterville, Coalinga, Reedley, Dinuba, Corcoran and Lindsay.

Region 11.—Regional Hospital: Salinas; Community Hospitals or Service Centers: Monterey, Hollister and King City.

Region 12.—Regional Hospital: Bakersfield; Community Hospitals or Service Centers: Taft, Wasco, Delano, Tehachapi, Mojave, Ridgecrest, Lone Pine, Bishop and Bridgeport.

Region 13.—Regional Hospital: Santa Barbara; Community Hospitals or Service Centers: Santa Maria, Paso Robles, Santa Paula, Ventura, Oxnard, San Luis Obispo and Lompoc.

Region 14.—Regional Hospital: San Bernardino; Community Hospitals or Service Centers: Redlands, Riverside, Corona, Blythe, Elsinore, Uplands, Indio, Banning, Palm Springs, Victorville, Barstow, Needles and Loma Linda.

Region 15.—Regional Hospital: San Diego; Community Hospitals or Service Centers: Escondido, National City, Brawley, Oceanside and Calexico.

Region 16.—Regional Hospital, and Teaching Center: Los Angeles; Community Hospitals or Service Centers: Santa Ana, Fullerton, Anaheim, Montebello, Culver City, Santa Monica, Beverly Hills, Burbank, Van Nuys, San Fernando, Palmdale, Glendale, Alhambra, Pasadena, Monrovia, Covina, Pomona, Whittier, Huntington Park, Compton, Long Beach, San Pedro, Torrance, Inglewood, Laguna Beach, Avalon and four within Los Angeles City and North County.

Your Association believes that the majority of areas in California are adequately supplied with physicians. The Committee on Rural Medical Service is working in cooperation with allied groups to improve the availability of medical service in the few rural areas still lacking such. The Committee on Hospitals is working with allied groups in an attempt to stimulate the development of additional hospital beds where they can be of most use to the sick.

Narcotics Warning

Calling attention to irregularities in the prescribing of narcotics by some California physicians and to what appears to be, in some instances, obvious negligence in complying with the provisions of Division 10, of the Health and Safety Code, (State Narcotic Act), F. Joseph O'Ferrall, Chief of the Division of Narcotic Enforcement of the California State Department of Justice has issued the following statement to the medical profession, as a warning:

"Henceforth all apparent irregularities will be investigated by the enforcement personnel of the Narcotic Division, under the Act. All triplicate copies of prescriptions issued by physicians throughout the State are forwarded to the Narcotic Division in accordance with Section 11166.11 of the Act. These copies are scrutinized and controlled by means of a key punch system and tabulations. Perusal of the tabulations discloses a definite uptrend in the quantity of narcotics prescribed as well as irregularities in the manner of prescribing and reveals the names of many persons receiving narcotics who have not been reported in accordance with the provisions of the law.

"The Narcotic Division believes, also, that some physicians are not making their own diagnoses in cases in which narcotics are prescribed, to determine whether or not such narcotics are indicated. It is incumbent upon every physician to dictate his own therapy and not accept the statement of the patient that narcotics are necessary.

"Instances have been noted in which there is an utter disregard of safeguards relating to the amount of narcotics prescribed for patients. Some physicians are on record as prescribing as much as 350 one-half grain Morphine tablets to a patient at one time. It is the contention of the Division that any patient ill enough to require that quantity of narcotics should have a physician in close attendance, who could prescribe for the condition as it exists at the time, and not issue a prescription for an excessive amount of narcotics. Of course, this does not apply in cases of malignancy which may be inoperable. In such cases the patient must be allowed such narcotics as the physician may deem necessary until the terminal status has been reached.

"The tabulations also reveal that there is considerable negligence on the part of physicians in reporting cases where narcotics have been prescribed, as required by Article 3, Section 11425 and 11426 of the State Narcotic Act. Report Cards are provided by the State Division on request, for the use of physicians in reporting cases where narcotics are required over a protracted period of time in the treatment of conditions wherein narcotics are indicated. Aside from being required by law, these reports are very important in checking on the activities of persons who do not have a pathological condition necessitating the use of narcotics but who impose upon ethical physicians in their efforts to procure narcotics to satisfy their addiction.

"Attention is especially called to the fact that ambulatory treatment of narcotic addicts is not permitted. A physician cannot treat a case of narcotic addiction in the patient's home. Such treatment must be given in a hospital or an institution approved by the Board of Medical Examiners, where the patient is at all times under restraint and control. (A list of approved institutions may be procured from the office of State Narcotic Division or the Board of Medical Examiners.) All treatment for narcotic addiction must be reported to the Division of Narcotic Enforcement and be in accordance with Article 2, Sections 11390 to 11395 inclusive, of the Act.

"The Division of Narcotic Enforcement has been cognizant for some time of the many flagrant irregularities involving the prescribing of narcotics. However, due to the limited personnel available, particularly pharmaceutical inspectors who could interview the medical profession with understanding, no drastic action has been taken except in a few very serious cases. A licensed physician and surgeon who violates the regulations regarding ambulatory treatment of addicts or otherwise violates the provisions of the State Narcotic Act is subject not only to criminal prosecution but may also have his license revoked by the Board of Medical Examiners.

"Although the Division of Narcotic Enforcement is primarily an enforcement unit it also acts as a service bureau, in that it stands ready at all times to counsel and advise the medical and pharmaceutical professions on any and all individual problems relating to narcotics. The Division of Narcotic Enforcement wishes to cooperate with the medical profession to the fullest extent but must also fulfill its obligation to the people of the State and enforce the provisions of the Narcotic Act. The ethical physician is, we know, desirous of complying with the law and will welcome any investigative program which may be instigated.

"Your attention is called, at this time, to page 7 of your 1946 Medical directory, under the caption '*Warning*,' which contains valuable information relative to the prescribing, administering and dispensing of narcotic drugs."

A copy of the State Narcotic Act will be furnished on request and any specific information desired may be obtained from the Division of Narcotic Enforcement, Department of Justice, 156 State Building, San Francisco 2, Telephone, Underhill 1-8700, Local 560, or 105 State Building, Los Angeles 12, Telephone, Madison 1271, Extension 755.

There are certain Federal Regulations with which the physician should also be familiar. Information concerning these may be obtained from Mr. R. W. Artis, District Supervisor, U. S. Bureau of Narcotics, 100 McAllister Street, San Francisco.

BOOK REVIEWS

COMMON CONTAGIOUS DISEASES. By Philip Moen Stimson, A.B., M.D., Assistant Professor of Clinical Pediatrics, Cornell University Medical College; Visiting Physician, Willard Parker Hospital; Director, Poliomyelitis Service, The Knickerbocker Hospital; Medical Director, The Floating Hospital of St. John's Guild. Fourth Edition, thoroughly revised. Published 1947. 503 pages with 67 illustrations and 8 plates, 6 in color. Flexible binding, $4.00. Lea & Febriger, Philadelphia.

This is a needed revision of a familiar work. It is written by a clinician of long experience in isolation hospitals. It does not pretend to be a reference work. It is a manual to be used on the spur of the moment by general practitioners, internists, pediatricians, public health officers and medical students. Nurses may be added to this list, so elementary does the author become at times.

The new chapter on antibiotics is a good summary of the indications and contra-indications for their use. The chapter of the general management of contagious diseases in the home and hospital is practically official for public health officers.

Active immunization procedures are not discussed as fully as most pediatricians require. On the other hand treatment is discussed in more detail than in many text books. The chapter on poliomyelitis is the best in the manual.

* * *

REHABILITATION THROUGH BETTER NUTRITION. By Tom D. Spies, M.D., From the Department of Internal Medicine, University of Cincinnati College of Medicine. 94 p., 50 Fig. Philadelphia and London: W. B. Saunders Company, 1947. Price $4.00.

Dr. Tom D. Spies is an indefatigable worker, a fluent talker and a facile writer who seems to love all three occupations. For 17 years he has devoted himself to the study of deficiency diseases, writing an increasing number of articles in medical journals. At present he is writing monographs, of which this is the second in a few months.

This monograph is concerned with the long-term application of the principles of nutritive therapy which make it possible for the malnourished to regain health and to perform work. It is largely a summary of his personal experiences, particularly of the studies at the Hillman Hospital in Birmingham, Alabama. It is worth-while reading for the physician interested in the problems of nutrition, even if the type of case encountered is generally different from that which one encounters in the Pacific Coast States.

The author arbitrarily excludes from consideration deficiencies of vitamin D and K and touches very lightly on microcytic anemia and non-tropical sprue for the reason that he has not seen much of these conditions. While this is commendable in that one can be sure of the author's personal knowledge about the subjects which he does discuss at length, it detracts from whatever value the book may have as a useful textbook on the diagnosis and therapy of the deficiency diseases as a whole. The signs and symptoms of those conditions which are taken up at length are well detailed. The long subclinical period found in all vitamin deficiencies is brought out well. The emphasis given to a 4,000 calory diet is misleading to physicians who work among a population not given to heavy manual labor—and, if followed, would certainly lead to a wide-spread obesity productive of as many difficulties as the prior malnutrition.

* * *

TUBERCULOSIS, AS IT COMES AND GOES. By Edward W. Hayes, M.D., F.A.C.P., Associate Professor of Tuberculosis, College of Medical Evangelists, Los Angeles, with Chapters by Laurence de Rycke, Ph.D. Second edition. May 1, 1947. Charles C. Thomas, Publisher, Springfield, Illinois. Price $3.75.

The second edition of this extremely useful little book on pulmonary tuberculosis written largely for the benefit of the patient is entirely revised and maintains the same high standard set in the first edition. Two excellent chapters entitled "Suggestions to Patients" and "Suggestions to Visitors" have been written by Dr. Laurence de Rycke, Ph. D. These are a distinct addition to the book. The diagrams illustrating collapse therapy are especially informative and render the book valuable in explaining to the patient measures later advocated by his own physician.

The page size has been enlarged and the type with it. The new edition is distinctly easier for a patient to read than the old one. The book may be highly recommended by physicians to their patients.

* * *

PERIPHERAL VASCULAR DISEASES. (Angiology). By Saul S. Samuels, A.M., M.D. Consulting Vascular Surgeon, Long Beach Hospital, Long Beach, New York; Attending Vascular Surgeon, Brooklyn Hospital for the Aged; Chief of the Department of Peripheral Arterial Diseases, Stuyvesant Polyclinic Hospital, New York; Fellow in Surgery, New York Academy of Medicine; Member of Committee on Surgery, New York Diabetes Association. Second Edition, 1947, pp. 85. Oxford Medical Outline Series. Oxford University Press, New York. Price $2.50.

In the preface to this second edition of his book, the author emphasizes the importance of assigning the entire responsibility for the care of patients with peripheral vascular disease to one individual "expertly trained in both medical and surgical phases of the subject, if progress in this field is to be made along present lines with a reduction in the number of cases requiring amputation and in the mortality rate."

This book is an outline for students and graduate physicians. The opening chapters briefly review the anatomy of the blood vessels and autonomic nervous system, classification of peripheral vascular diseases and symptomatology. Then follows the most significant section of the book devoted to a consideration of physical signs of arterial occlusion, diagnostic tests and the conservative treatment of obliterative arterial disease. The author has had a vast experience in this field. Emphasis is placed on simpler forms of prevention and treatment rather than on the use

of mechanical means of increasing the circulation to the extremities. The use of intravenous injections of 2 per cent sodium chloride solution 300 cc., three times a week, is strongly advocated. Intermittent venous occlusion, suction and pressure machines and sympathectomy are mentioned only to condemn their use. Complete rest in bed, abstinence from smoking, preservation of natural warmth, and scrupulous care to the extremity comprises the main treatment for occlusive vascular disorders. The author has rightly emphasized the importance of these conservative measures. Amputation of the leg, particularly in patients with Thromboangiitis Obliterans, is indicated only when there has been destruction of the weight-bearing portion of the foot.

The remainder of the book is devoted to considerations of various vascular disorders, vasospastic, congenital, and traumatic. The outlines are too short to be of value and there are some aspects which are not considered. For instance, in the discussion of venous thrombosis no mention is made of deep venous thrombosis of the calf, phlebothrombosis. Again, in the treatment of aneurysms, proximal ligation of the artery or extirpation of the sac is advocated. No mention is made of intrasaccular obliteration with preservation of the collateral vessels.

This book is valuable as an outline of peripheral vascular diseases chiefly in the diagnosis and conservative management of patients with obliterative arterial disorders.

* * *

ROENTGEN INTERPRETATION. By George W. Holmes, M.D., Board of Consultation, the Massachusetts General Hospital and Clinical Professor of Roentgenology Emeritus, Harvard Medical School, and Laurence L. Robbins, M.D., Radiologist-in-chief to the Massachusetts General Hospital and Associate in Radiology, Harvard Medical School. Seventh edition, thoroughly revised, published 1947. Octavo, 398 pages, with 266 illustrations. Fabrikoid, Lea & Febiger, Philadelphia. Price $7.00.

This familiar text reappears in slightly modernized dress and with a new co-author. In previous editions the cuts were reproduced from positive prints and were therefore the reverse of films as handled by the physician or resident. A gradual change is being made to negative illustrations and the new illustrations in this edtion are of such type. This results in a little confusion, but is undoubtedly a step in the right direction. In subsequent editions, it is hoped complete revision to negative prints will take place.

Much of the text is unchanged, and has been reviewed in previous issues of this journal. The manual can be recommended to all residents in hospitals, to many senior students, and to many practitioners. We believe it is of a special use for general practitioners in smaller communities who do some of their own roentgenography.

It is to be doubted if extensive bibliographies at the end of each section are essential for an elementary text of this type. The continued reproduction of Elsberg and Dyke's chart of alleged normal interpedicular distances is of questionable use, in view of published results obtained with this chart. On page 244 appears a sentence "The films of most adult lungs show a certain amount of thickening of the bronchial markings as a result of previous infection. . . ." We believe the time has come for reliable texts to be a little more precise in the use of the terminal "bronchial" markings. Undoubtedly the authors mean bronchovascular or vascular markings. It is well known that the bronchi contribute only a small amount to the shadows seen in the lungs proper under normal circumstances.

Diagnostic roentgenography now encompasses such a wide field that the authors must be congratulated on their continued ability to compress so much information into so small a space.

* * *

DISEASES OF THE NERVOUS SYSTEM. By F. M. R. Walshe, M.D., D.Sc. F.R.C.P. (Long.), F.R.S., D.Sc. (Hon.), Nat. Univ. Ireland. Fifth Edition. The Williams and Wilkins Company, Baltimore. Copyright 1947. Price $4.50.

A small, compact textbook of clinical neurology which presents the underlying anatomical and clinical syndromes in a clear and concise manner.

The volume is designed primarily to present to medical students a complex subject in a simplified form. It is an excellent book for the use of medical students or for those individuals who wish a source of ready reference.

Although the anatomical and clinical diagnostic portions of the volume are excellent, the portions dealing with special diagnostic procedures and treatment particularly those pertaining to the surgical aspects of certain neurological lesions are at times incomplete. The chapter dealing with sciatic and brachial neuritis makes no mention of pantopaque as used for spinal myelography, and in the portion treating brachial neuralgia the possibility of a protrusion of the intervertebral disc in the cervical region as an etiological factor is not mentioned. The chapter on arterial aneurysms of the circle of Willis with subarachnoid hemorrhage leaves one with the impression that this lesion is followed by a complete recovery in a high percentage of cases which is contrary to the present accepted opinion. In the chapter dealing with hypertension there is very little emphasis placed on proper examination and evaluation of the funduscopic findings, which should be presented even though this is a book primarily dealing with neurology. Here again from the standpoint of treatment the possibility of sympathectomy as a therapeutic measure is not mentioned.

In spite of these minor therapeutic omissions the author has been highly successful in condensing a vast amount of material and information into one small volume which presents the essential, fundamental principles of neurology in a manner which can be highly recommended to those beginning a study of neurology.

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A HANDBOOK ON DISEASES OF CHILDREN. Including Dietetics & the Common Fevers. By Bruce Williamson, M.D., Edin., F.R.C.P., London. Fifth Edition. 1947. The Williams and Wilkins Company, Baltimore. Price $4.50.

This handbook contains both errors of commission and errors of omission. It is not up to date. It cannot be recommended.

MEDICAL JURISPRUDENCE

OPERATIONS UPON PERSONS LEGALLY INCOMPETENT TO CONSENT; RESTORATION TO CAPACITY TO CONSENT

PEART, BARATY & HASSARD, *San Francisco*

It is a general rule of law that a physician or surgeon cannot operate upon a person without that person's express or implied consent, or if the person is legally incompetent of consenting, then without the express or implied consent of one legally competent to consent for him.

Two classes of persons who are, by law, incompetent to give a legally valid consent are minors and mentally incompetent adults. Consent to operate upon such persons must be obtained from the person duly appointed to act as guardian, or in the case of minors with living parents, from the parents. This discussion will not be concerned with a situation where a physician or surgeon acts in cases of emergency to save life or limb.

A person who has been declared legally incompetent cannot give a valid consent to an operation. If a guardian has been appointed, then the guardian can consent to the operation. It often becomes important to determine whether a person who has been declared incompetent has been restored to competency, for if he has been so restored, he can, of course, give a valid consent and the physician or surgeon will be protected. Under sections 1470, 1471 and 1472 of the California Probate Code any person who has been declared legally insane or incompetent may apply, by petition, to the superior court of the county in which he was declared insane, or from which letters of guardianship were issued, to have the fact of his restoration to capacity judicially determined. After a trial if it is found that the person in question is sane and capable of managing and taking care of himself and his property, his restoration to capacity is adjudged and the guardianship of such person ceases. A restoration to capacity can be thereafter evidenced by a certified copy of the judgment of restoration.

Where a person has been committed to a state institution and is thereafter released, it is often difficult for that person to prove restoration to capacity and hence the physician or surgeon should proceed with caution. Under section 6728 of the California Welfare and Institutions Code, the superintendent of a State hospital, on filing his written certificate with the Director of Institutions, may discharge any patient who, in his judgment, has recovered. This in and of itself, however, does not restore a person to legal competency. Section 629 of the California Welfare and Institutions Code provides that a copy of the certificate of discharge may be certified and filed with the clerk of the superior court of the county from which the person was committed. Section 6729 further provides that "such certified copy of such certificate and the record of the same shall have the same legal effect . . . as a judgment of restoration to capacity made under the provisions of sections 1470, 1471, and 1472 of the Probate Code." Therefore, if a person has been committed to a state institution and thereafter is released, a physician or surgeon before accepting such person's consent to an operation or other treatment, should insist that the person produce a certified copy of the certificate of discharge with evidence of its filing with the Director of Institutions and of the filing of the certificate of discharge with the clerk of the superior court of the county from which the person was committed. If these requirements are not complied with, then legally the patient is still incompetent and therefore unable to give a valid consent to any operation.